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A.M.A. ARCHIVES OF

# DERMATOLOGY

Art for Art's Sake in Medicine
*Werner Jadassohn*

The Association of Psoriasis with Blood Groups
*G. K. Hargreaves and F. F. Hellier*

Carcinoma of Apocrine Glands
*G. F. Kipkie and M. Daria Haust*

Atypical Features in Familial Benign Chronic Pemphigus
*Thomas W. Lyles, John M. Knox, and J. B. Richardson*

Lichenoid Eruptions Following Contact Dermatitis
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Dermatitis from Metal Spectacles
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A Unique Case of Trichorrhexia Nodosa—"Bamboo Hairs"
*Earl W. Netherton*

Woolly Hair Nevus
*Charles F. Post*

A Critical Evaluation of the Effect of Steroid Lotions on Inflammatory Dermatoses
*Ira Leo Schamberg, Samuel I. Askovitz, and Marvin Greenberg*

On the Evaluation of Paired Comparison Studies
*S. I. Askovitz*

Chlorothiazide in Acne
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Dermatitis Medicamentosa Due to Diuril (Chlorothiazide)
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Epidemic Due to Microsporum Canis
*Edward H. Ferguson*

Correspondence

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Prof. Dr. J. J. Zoon
Geoffrey Rake, M.D.
Loretta Joy Cummins, M.D.

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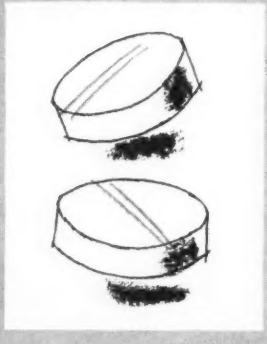

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# ARCHIVES OF DERMATOLOGY

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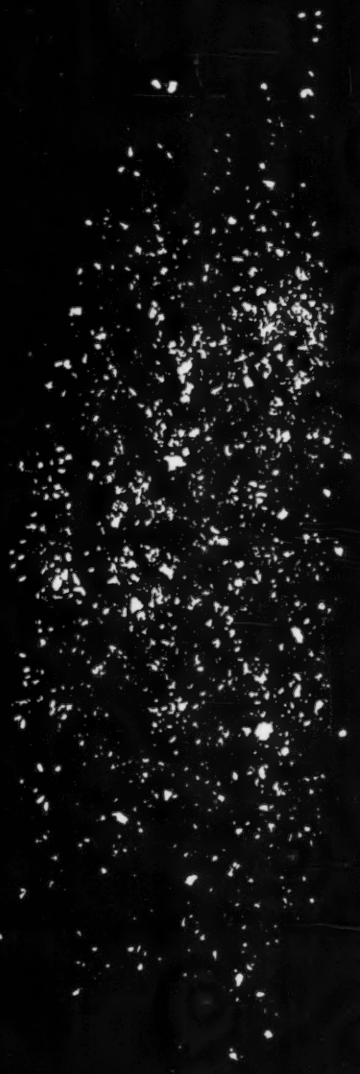

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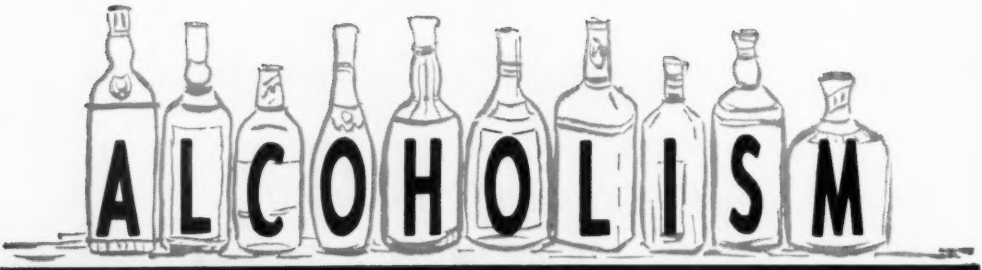


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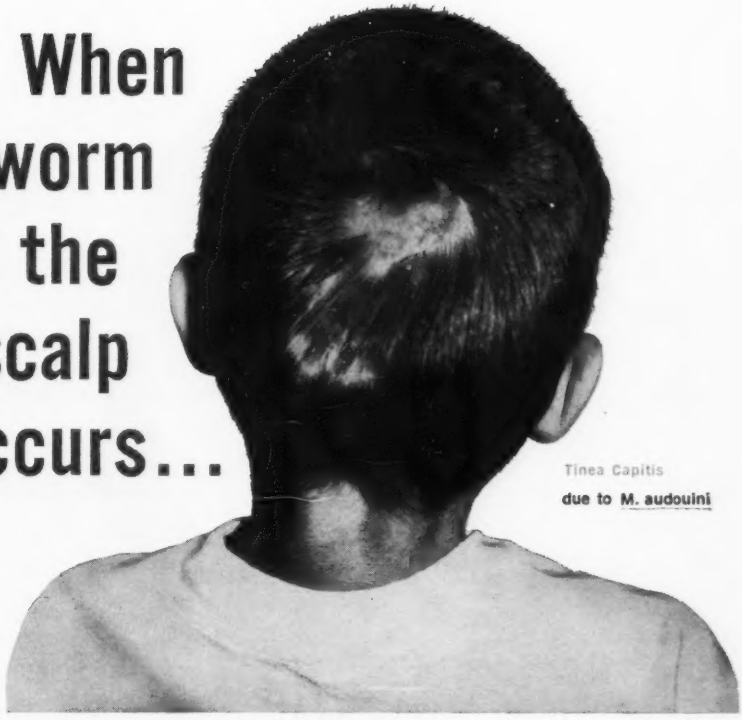

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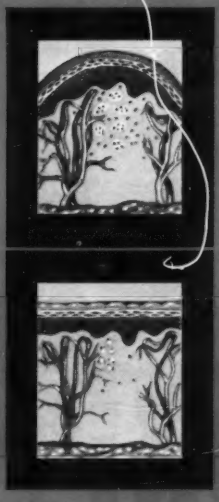
# "prompt remissions"[1]



"...when the tar-steroid cream TARCORTIN was prescribed for patients presenting very acute episodes of atopic dermatitis, contact dermatitis, psoriasis, chronic infectious eczematoid dermatitis, and other eczematous dermatoses...we were able to achieve prompt remissions..."[1]

1. Welsh, A. L., and Ede, M.: J.A.M.A. 160:158, 1956.

Additional Clinical Publications on Tarcortin:

Clyman, S. G.: Postgrad. Med. 21:309, 1957 • Bleiberg, J.: J. M. Soc. New Jersey 53:37, 1956 • Abrams, B. P., and Shaw, C.: Clin. Med. 3:639, 1956 • Bleiberg, J.: Am. Practitioner 8:1404, 1957

**NEW TARCORTIN LOTION**
excellent for lesions of head and hands
supplied—plastic squeeze bottles ½ ounce

# TARCORTIN®

Cream — Hydrocortisone 0.5% and Special Coal Tar Extract 5% (TARBONISE®) in a greaseless, stainless vanishing cream base. In tubes of 7 gm. and 1 oz.

ALSO AVAILABLE: FOR DRY SCALY ECZEMAS, AND WHEN INFECTION IS PRESENT OR ANTICIPATED

# NEO-TARCORTIN®

Ointment — Hydrocortisone 0.5%, Neomycin (as Sulphate) 0.35% and Special Coal Tar Extract 5%. In tubes of 7 gm. and 1 oz.

R&C REED & CARNRICK Jersey City 6, New Jersey

# dermatoses

Kenacort with its unsurpassed antiallergic, anti-inflammatory and antipruritic activity quickly alleviates the itching, erythema, and irritation in most inflammatory skin conditions.

The table shows the effectiveness of relatively small doses of triamcinolone (Kenacort) in the treatment of some common dermatoses.

Summary of Clinical Effects of Triamcinolone on Dermatoses in Fifty-one Patients.[1]

| TYPE OF LESION | HELPED, NO. | NOT HELPED, NO. |
|---|---|---|
| Chronic eczematous eruptions, including atopy | 14 | 5 |
| Localized neurodermatitis | 4 | 2 |
| Contact dermatitis | 6 | 6 |
| Seborrheic dermatitis | 9 | 0 |
| Alopecia areata | 4 | 1 |

In psoriasis, Kenacort should be reserved for those patients suffering from acute, extending or severe chronic forms of the disease. The authors report prompt and dramatic relief in 36 of 60 such patients treated with 12-16 mg. per day.

Kenacort is indicated in the treatment of dermatoses, asthma, allergies and arthritis —

**KENACORT**
Squibb Triamcinolone

**with a low incidence of gastric disturbance** [1,2,5,6]
**without salt and water retention** [1-8]
**with no potassium loss** [4, 8]
**without unnatural psychic stimulation** [1,2,5]
**with no adverse effect on blood pressure** [1,2,4,5,7]
**on a low daily dosage range** [1,2,6,7]

*Supply:* Scored tablets of 1 mg. and 2 mg.—bottles of 50. Scored tablets of 4 mg.—bottles of 30 and 100.

1. Shelley, W.B.; Harun, J.S., and Pillsbury, D.M.: J.A.M.A. *167*:959 (June 21) 1958. 2. Sherwood, H., and Cooke, R.A.: J. Allergy *28*:97 (March) 1957. 3. Boland, E.W.: Geriatrics *13*:190 (March) 1958. 4. Hellman, L., and others: A.M.A. J. Dis. Child. *94*:437 (Oct.) 1957. 5. Hartung, E.F.: J.A.M.A. *167*:973 (June 21) 1958. 6. Feinberg, S.M.; Feinberg, A.R., and Fisherman, E.W.: J.A.M.A. *167*:58 (May 3) 1958. 7. Friedlaender, S., and Friedlaender, A.S.: Antibiotic Med. & Clin. Ther. *5*:315 (May) 1958. 8. Dubois, E.L.: J.A.M.A. *167*:1590 (July 26) 1958.

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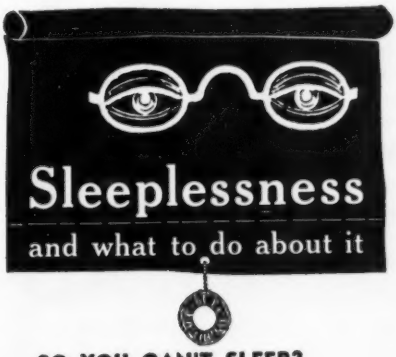


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out of
**106**

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successfully
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*Miller, J. M.; Godfrey, G. C.; Ginsberg, M., and Papastrat, C. J., in Surgical Service, V. A. Hospital, Fort Howard, Maryland: Postgrad. Med. *22*:609, 1957.

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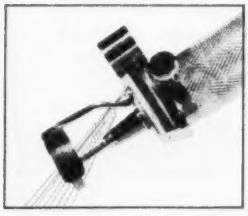

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*A.M.A. Archives of Dermatology, April 1955*
*Ref.: Wilson, J. W.; Luikart II, R.; Ayres III, S., Reprints available*

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# breaking the tolerance barrier in dermatoses

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**takes the "sting" out of coal tar . . .**
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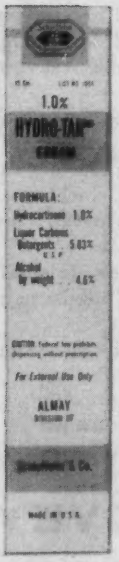
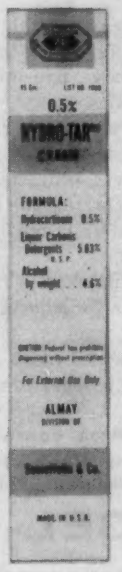
*Dosage:* Apply topically by gentle massage to affected areas 3 or 4 times a day . . .

0.5% for moderately severe dermatoses or maintenance–1.0%. for severe dermatoses.

*Supplied:* 15 gm Tubes in 0.5% and 1.0% strengths.

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"Meti" steroid benefits directly on dermatoses

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ease of application
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Each spray can contains 50 mg. of prednisolone. A 3-second spray delivers approximately 0.5 mg., an amount sufficient to cover an area about the size of the hand.

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either alone or complicating physical illness

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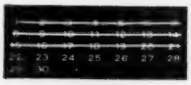
# *RAPID HEALING...3 WEEKS*



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**MALT SOUP EXTRACT**

More and more physicians are telling us of the successful results from treating Pruritus Ani orally with Borcherdt's Malt Soup Extract. The intractable itching disappears in three or four days and the perianal skin becomes normal in three or four weeks. Even stubborn cases of many years standing usually yield or show marked improvement.

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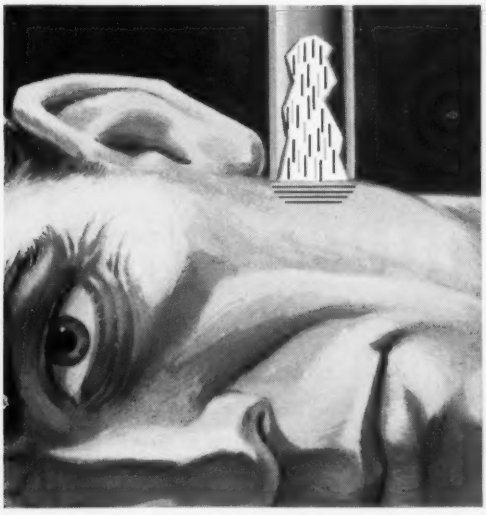

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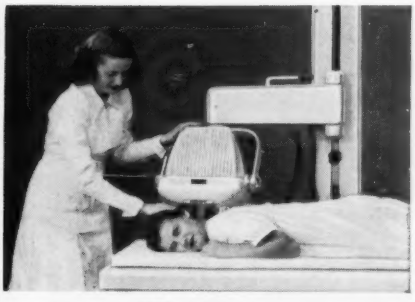

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Silicote provides an important advance in protecting skin from dry and aqueous irritants—prophylactically to prevent skin maceration, and therapeutically to exclude water, soap, and other substances from dermatoses that may be aggravated by them.

Clinical tests show that Silicote provides excellent protection against soap and water and soluble cutting oils.[1]

The protective property of Silicote is purely mechanical. Protective efficiency is necessarily determined by the nature and frequency of exposure. Frequency of application should be adjusted to provide adequate protection with minimum dosage.

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CONTRAINDICATIONS: Do not use on weeping or infected areas.

In Housewife's Eczema
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Diaper Rash
Chronic Dermatoses
Aggravated by Soap
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**SILICOTE CONTAINS**
30% dimethicone (silicone) in a specially prepared petrolatum base. Contains no water-soluble ingredients.

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1. Shaw, J. M., and Crowe, F. W.: Skin Protective Ointments. Arch. Dermat. & Syph. 71: 379, 1955.

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In subacute and chronic dermatoses, "especially where an inflammatory reaction was accompanied by increased scaling and lichenification with secondary infection such as is seen in seborrheic dermatitis, atopic dermatitis, contact dermatitis, and neurodermatitis."

*—Rein, C. R., and Fleischmajer, R.: Personal Communication.*

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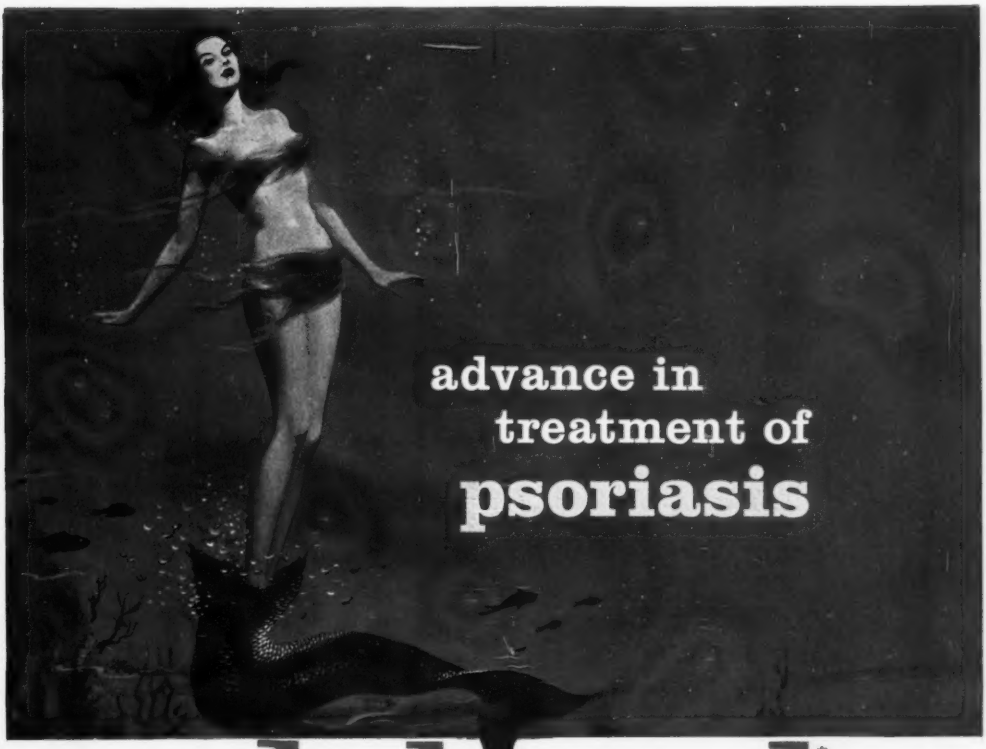


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**Affords keratin-dispersing action**[1]: Keratolytic, removes nonviable tissue, promotes healing.

**Successful results ranging to complete clearing** obtained[2-4] in patients with: • scalp-to-toe psoriasis • psoriasis of many years' duration • psoriasis involving tender areas.

**Treatment-fastness rarely occurs:** Recurrences (when treatment is discontinued) clear up again on resumption of therapy.

**Well tolerated:** Even when applied to lesions in anogenital and submammary regions.[2] Potential hazards of other therapies – mercury, arsenic, corticosteroids, x-rays – are avoided.

**A noteworthy advance cosmetically:** Nongreasy, nonstaining; vanishes on application to the skin. May be used freely on the scalp.

**Application:** Rub into lesions 2 to 4 times daily as indicated. Where heavy scaling or crusting occurs, the usual bath, to soften and facilitate removal of scale, is recommended before applying lotion.

Residual redness and pigmentation may remain up to several months but will eventually disappear. Once the condition is under control, daily to weekly application may prove satisfactory for maintenance.

In some cases, a seeming excessive scaling and drying may occur during therapy. This is an occasional phase of the healing process and usually precedes improvement. Patients should be advised of this and encouraged to continue therapy.

**Formula:** Allantoin 2% and special coal tar extract 5% in a lotion base.

**Supplied:** Bottles of 8 fl. oz.

(1) Flesch, P.: Reported Conf. N. Y. Academy Science May 9, 1958 (In Press). (2) Bleiberg, J., and Saltzman, J. A.: Clin. Med. *5*:485 (Apr.) 1958. (3) Bleiberg, J.: Reported Conf. N. Y. Academy Science May 9, 1958 (In Press). (4) Clyman, S. G.: Reported Conf. N. Y. Academy Science May 9, 1958 (In Press). *Trademark

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For a time-saving and convenient method of wet compress therapy dermatologists are turning to DERMPAK Therapeutic Gloves when treating eczematous processes of the hands.

DERMPAK Gloves are widely accepted because they not only conserve valuable personnel time but meet with exceptional acceptance by the patient.

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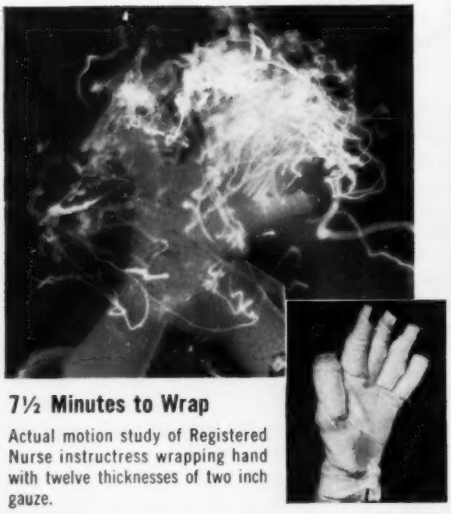

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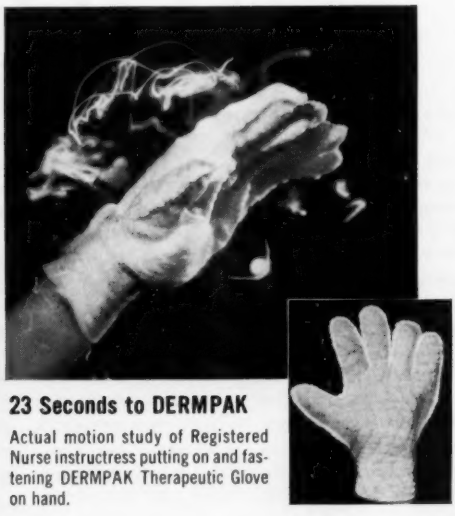
Actual motion study of Registered Nurse instructress wrapping hand with twelve thicknesses of two inch gauze.



**23 Seconds to DERMPAK**

Actual motion study of Registered Nurse instructress putting on and fastening DERMPAK Therapeutic Glove on hand.

**DERMPAK CORPORATION**
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*AGGRAVATES...*

*PROLONGS*

## *DERMATITIC CONDITIONS*

Soap, because of its high alkalinity, can be a primary cause of skin irritation. Or it can aggravate a dermatitic condition already present...make it worse...and even prolong it. Lowila is soap free...does not contain alkali, fatty acids or perfumes. Lowila cleanses tender or dermatitic skin without irritation...maintains the normal acid mantle of the skin...creates an environment favorable to therapy and normal healing.

Lowila should replace your patients' regular bar soap for washing, bathing and shampooing. It easily works into a rich, gentle lather in both hard and soft water.

*Soap irritation wastes sound dermatologic therapy . . . recommend Lowila Cake.*

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*use* **LOWILA® CAKE**

*to cleanse without irritation*

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Your approval is our only criterion of success. We advertise Oilatum Soap to dermatologists *only*. That is why we note with appreciation the ever-increasing demand for our product as an effective aid to "dry skin" therapy.

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A.M.A. ARCHIVES OF
DERMATOLOGY

# Art for Art's Sake in Medicine

WERNER JADASSOHN, M.D., Geneva, Switzerland

In the 90th Psalm we find the words: "The days of our years are threescore years and ten; and if by reason of strength they be fourscore years, yet is their strength labour and sorrow; . . ." "Yet is their strength labour and sorrow . . ."

In Luther's version this reads: "but his life has been worthy if it has been a life of toil and care."

The life of Howard Fox was fourscore years, and it was indeed worthy, for it was a life of toil and care: toil and care for his patients, his students, and the science of dermatology.

I myself never had the good fortune to know this great dermatologist, physician, and man. But I know what his friends, and those who worked under him and with him, thought of him; I am very much alive to the great honor I have in delivering this First Memorial Lecture, and I am deeply indebted to all those who have been responsible for this invitation. I know that it is due less to my own merits than it is to my old friendship with Marion Sulzberger.

With your leave now I shall broach my subject: "Art for Art's Sake."

Toulouse-Lautrec once painted an advertisement for the Moulin Rouge in Paris. It is a masterpiece, but is it Art? Does Art dare to have a practical purpose, or does it exist only for its own sake?

If we extend this motto or, if you prefer, this slogan that I have chosen for this lecture and apply it to the field of our own special interest, it becomes "Science for Science's Sake." To put a question mark after this sentence and to try to defend it might be asking for trouble. For some people, Science is a sublime goddess; for others, Science is a cow that provides us with butter. Both Goethe and Schiller expressed themselves in these severe terms against those who are engaged in the applied sciences, trying to put science to practical purposes—such as practical dermatology, to mention the branch which interests us most closely.

When, in 1925, I first heard about my future chief, Prof. Bruno Bloch, everybody sang his praises. Among these there was one item that impressed me but little. It appeared that Professor Bloch was investigating, and with what burning zeal, the formation of pigment. That, they explained, is pure science: to investigate the mechanism of pigmentation without any ulterior thought as to practical usefulness. I had just done three years of surgery under the direction of Professor Wildbolz, and it mattered little to me whether or not there was a special enzyme, dopa oxidase, which transformed dopa, dihydroxyphenylalanine, into melanin, the brown pigment of the skin. I must confess, therefore, that when I became assistant to Professor Bloch and he

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proposed that I take part in his work on pigmentation I did what my collaborators do to me today when they are not enthused by my proposals: I offered passive resistance.

In 1930 von Szent-Gyorgyi discovered ascorbic acid (vitamin C) and Reichstein synthesized it. Quite suddenly the work of Professor Bloch seemed to have acquired a practical importance. Pigmentation, according to Bloch, was due to an oxidase. Therefore, if one wanted to avoid or remove a pigmentation, it seemed logical to administer a well-tolerated, essentially natural, and physiological reducing substance, ascorbic acid. Avitaminosis is rare among us today, and now that we had the medicament we ought to look for the illness, as Fourneau once said. Chloasma uterinum, a condition very common among pregnant women and which does not always disappear after delivery, upsets women considerably. It is even more serious in the case of a chloasma virginum, which gives rise to unfounded suspicions. It thus became the practice in those days to give large doses of ascorbic acid in all cases of hyperpigmentation, especially in cases of chloasma. Doctors did not agree as to the usefulness of this treatment. As for myself, I did not find the results very convincing, but it is difficult to judge when there are so few cases on which to base one's opinion. It was this practical problem which led me to take an interest in hyperpigmentation.

Lipschütz had shown that when guinea pigs with lightly pigmented nipples were given estrogens the nipples became black—as if they had been touched up with India ink to make them photograph the better. Here we had a hyperpigmentation which, according to Bloch, corresponded to chloasma uterinum. Figure 1 shows a case of chloasma in a medical student who put an estrogen-containing cream on his forehead, hoping that it would produce hair growth at the frontal and temporal margins of his scalp. Schaaf and I carried out the experiment of trying to prevent, by injections of an ascorbic acid preparation (Redoxon), the pigmentation of the nipples provoked by estrone. The result was a complete failure, and in consequence we stopped our attempts at giving ascorbic acid to women with chloasma uterinum, thereby effecting, at that time, a considerable economy. What we had wanted to show was that Bruno Bloch's experiments on pigmentogenesis, carried out without any thought as to their practical usefulness, had seemed to have acquired a practical value, but this was later belied by subsequent laboratory experiments. But that is not the end of the story. Now, more than 30 years after the beginning of Bruno Bloch's experiments, his ideas have been slightly

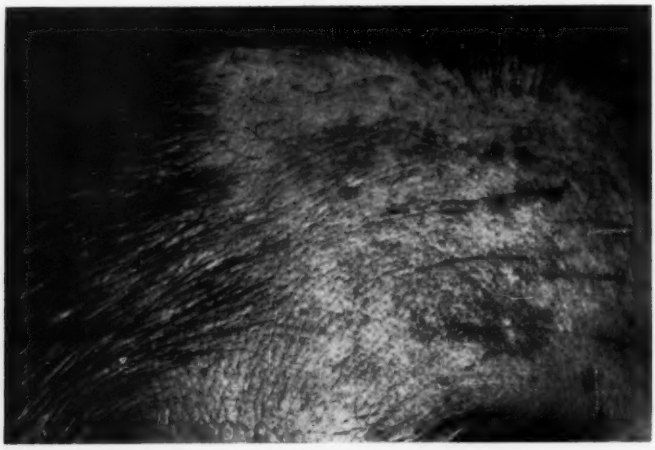

Fig. 1.—Chloasma in a man who applied an estrogen ointment to grow some hair.

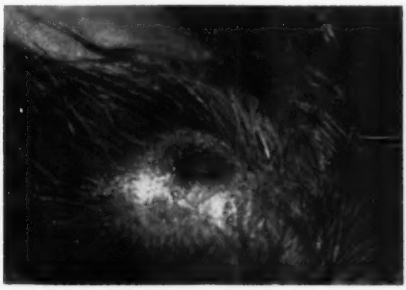

Fig. 2.—Pigmented guinea pig nipple before treatment.

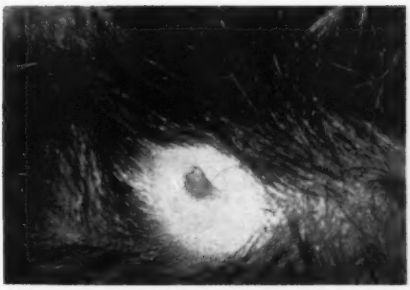

Fig. 3.—The nipple in Figure 2 after daily application of monobenzone ointment. Depigmentation of the nipple and the areola.

modified, it is true, but that does not detract from the work of Bloch and his collaborators. Once again his experiments seem

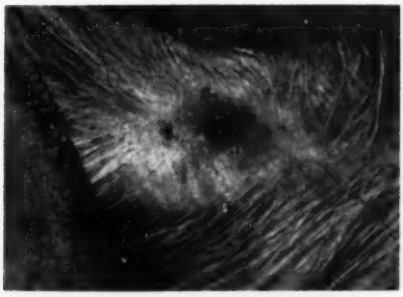

Fig. 4.—Pigmented guinea pig nipple before treatment with estrogen and monobenzone.

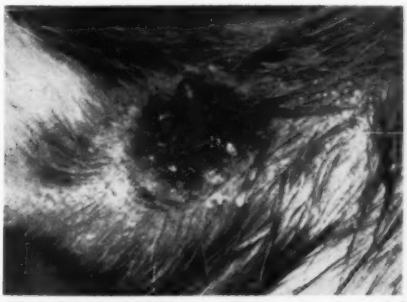

Fig. 5.—The nipple in Figure 4 after daily applications of monobenzone ointment and estrogen injections. No inhibition of pigment formation.

to have acquired a practical interest. Hyperpigmentation is once more being treated by reduction, but now the reducing substance is applied *in loco*. These experiments, inaugurated especially by American workers, have given more or less encouraging results, although their techniques have not been quite perfected. My collaborators have been sufficiently curious to check these experiments at the level of the guinea-pig nipple. So far, three conclusions can be drawn:

1. If monobenzone *ointment* (marketed under the name Benoquin), which contains the benzyl ether of hydroquinone, is applied every day to a highly pigmented nipple and areola, the pigmentation disappears in 28 days (Figs. 2 and 3). This has been verified macroscopically and microscopically. Except for some acanthosis, pathological lesions have not been produced. The application of a 5% *solution* of the benzyl ether of hydroquinone was not followed by depigmentation.

2. In the second series of experiments, we used guinea pigs with only slightly pigmented nipples. The monobenzone ointment

Fig. 6.—Nipple and areola partially dipigmented by application of monobenzone ointment.

was applied daily for four weeks, and, from the first day, we injected estrogens. These latter caused increased pigmentation of nipple and areola, and this increased pigmentation was not prevented by the monobenzone ointment (Figs. 4 and 5). The ointment, therefore, did not prevent pigmentation in statu nascendi.

3. In one guinea pig which had received no estrogen we were not able to obtain the depigmentation with monobenzone, and in another we obtained only a partial depigmentation. The top of the nipple and the areola became white, while the base of the nipple remained black (Fig. 6). From these experiments there arises a very interesting problem: Do there exist two kinds of pigment, one reacting to the benzyl ether of hydroquinone and another not reacting to this compound?

I have just said that the method of depigmentation by such substances as the benzyl ether of hydroquinone has not yet been perfected. I think that I have been able to show that it is possible, even probable, that experiments on guinea pigs will make easier the eventual experiments on humans, whose theoretical interest and practical purpose are beyond dispute.

Another problem, a very important one, also founded on Bruno Bloch's ideas, is that of judging the malignancy of a melanoma. It is to your fellow countrymen Fitzpatrick and Lerner that the credit is due for having undertaken experiments in this field with highly modern methods. Fitzpatrick told the 11th International Congress, at Stockholm: "During the past four years we have developed methods to define the dynamics of human tyrosinase present in various normal melanocytes and benign and malignant melanocytes (malignant melanoma)."

Dermatologists the world over are following these experiments with the liveliest interest, for melanoma, that extremely malignant tumor, has a great practical interest.

What I wanted to show is that the experiments of Bruno Bloch on pigmentation, carried out without any thought as to their practical usefulness, have, after more than 30 years, acquired a practical potential. But the practical problems raised here, in their turn, raised a large number of theoretical problems.

It may seem a trifle bold on my part to speak here at New York University of our experiments on perspiration, here where Sulzberger, Herrmann, and their collaborators have specially dedicated themselves to fundamental studies in this field. But this lecture is not going to be followed by a discussion, and, even if it were, I should not be much put out, seeing that our experiments are not carried out in competition. It is not very astonishing that good friends should have common interests.

According to Hesiod, the gods put sweat before success. But, as I once said in a lecture, that is not why I have taken an interest in the question of perspiration. It is about 15 years since I was struck by the fact that medical students were very interested in sarcoidosis. They had picked up some rather detailed ideas concerning this illness. But in our university it is one of our most important responsibilities to train doctors for the general practice of medicine in small villages. That is why, in my classes, I talk almost exclusively about those illnesses which are the commonest and most important for the general practitioner. I always explain that skin conditions which are often not dangerous are nevertheless very unpleasant for the sufferer. I had already so often used the skin disease acne vulgaris as an example of this that once, when we were discussing sarcoidosis, I wanted to give them another example, and I spoke to my students about hyperhydrosis. I told them how many women suffered not only from malodorous armpits but equally from the spoiling of their clothes by axillary perspiration. I told them about moist hands, which are so unpleasant to shake (a matter which is much more important in Europe

Fig. 7.—Perspiration test in hyperhidrosis of the hand. Treated side, left; nontreated side, right.

than in the United States, for Europeans are much more given to handshaking). I spoke to them about plantar hyperhydrosis and its importance in military service. But when I came to speak about treatment I was rather embarrassed, for I found that there was very little I knew about it, and I decided that we ought to try to find out more. We therefore worked out tests designed to measure axillary perspiration and others to measure palmar and plantar perspiration (Fig. 7). We also worked out tests for other parts of the body after the application of pilocarpine by iontophoresis. From these tests we found that the addition of a wetting agent to aluminum chloride increases its antiperspirant action. We could now make active preparations—aqueous solutions for the axillae and creams for the hands and the feet.

Later we used these tests for purposes other than to study the effects of therapeutic agents. It seemed to us that we lacked a great deal of theoretical knowledge in the field of perspiration. I cannot tell you of all the different problems that my collaborators investigated. I shall describe only three. A clinical case gave rise to our first investigation. It concerned a young girl who had not only an exceptional hyperhydrosis of the hands but also a very strong hyperhydrosis of the feet and axillae, and, besides that, she had a very marked lacrimal secretion. We wanted to know if there was any relationship between any or all of the four secretions; in other words, if, in general, the strong perspiration of the hands was more likely to go with strong perspiration of the feet and axillae as well as with an exaggerated lacrimal secretion. An experiment of this kind is not as easy to carry out as it would seem to be at first sight. Without the aid of mathematical statistics, it is impossible to come to a satisfactory conclusion. What makes this problem difficult, even for the mathematician or biostatistician specializing in this field, is the elimination of the effect of age. I shall have a word to say in a moment about the influence of age on these secretions.

We were able to show only one relationship—that between palmar and plantar secretion—a conclusion which was not without its theoretical interest. I give you this example to show you how much importance I attach to mathematical statistics in scien-

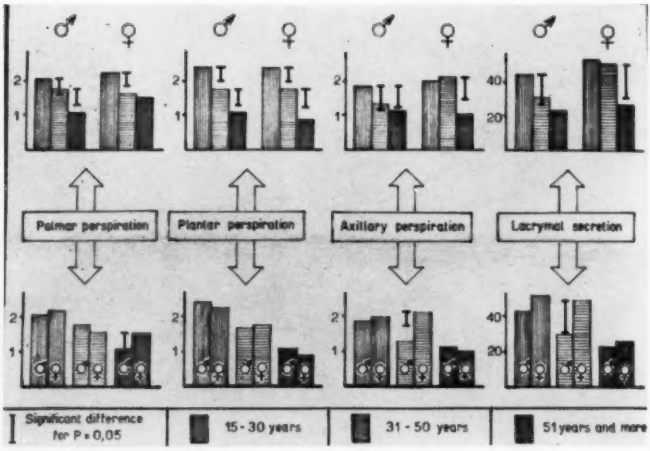


Fig. 8.—Variations of perspiration and lacrimal secretion according to age and sex.

tific work. I know that mathematical statistics can be a double-edged sword. I know and appreciate the little American book entitled "How to Lie with Statistics." But in the hands of the specialist, working seriously, mathematical statistics are not only useful; they are indispensable.

In the matter of the influence of age and sex, we plotted graphs showing the intensity of perspiration in the hands, feet, and axillae. We took three age groups: 15 to 30, 31 to 50, and over 50. All these secretions diminish with age, and, according to our graphs (Fig. 8), we can say at about what age this diminution occurs but without great precision. You will see that the lessening of perspiration of the palms and the soles does not necessarily take place at the same periods of life as the lessening of perspiration from the axillae. The graph shows that there does not seem to be any significant difference between the two sexes as far as perspiration is concerned, with the *notable exception* of perspiration from the *axillae* in persons between the ages of 31 and 50 (a finding confirming the one of Franz Herrmann and Sulzberger).

The third problem came to light in the course of other experiments; we had some failures in achieving antiperspirant effects with aluminium chloride. When the aluminium chloride solution was applied to the skin of the arm of some persons, it did not prevent the perspiration caused by the iontophoresis of pilocarpine. These persons were for the most part over 60 years old!

These experiments on perspiration, which have engaged us for a number of years and to which the staff of the dermatologic clinic of Geneva has devoted much labor, were undertaken because we set ourselves a purely practical problem: the treatment of hyperhydrosis. We think that we have made some progress in this field. And then, quite naturally, we came to the point where we began to use for purely theoretical investigations the tests which had been worked out primarily for practical ends.

We examined (1) the relationship between sweat secretions in different parts of the body and (2) the influence of sex and age on palmar, plantar, and axillary perspiration; we found the curious phenomenon that aluminium chloride acts against perspiration very frequently before the age of 60 but almost never after that age. We believe that we have made a contribution to the physiology of perspiration, but is it a purely theoretical one? The influence of age and sex is certainly not.

You must have noticed, not without some amusement, that in discussing the question mark after "Art for Art's Sake" and "Science for Science's Sake" I have

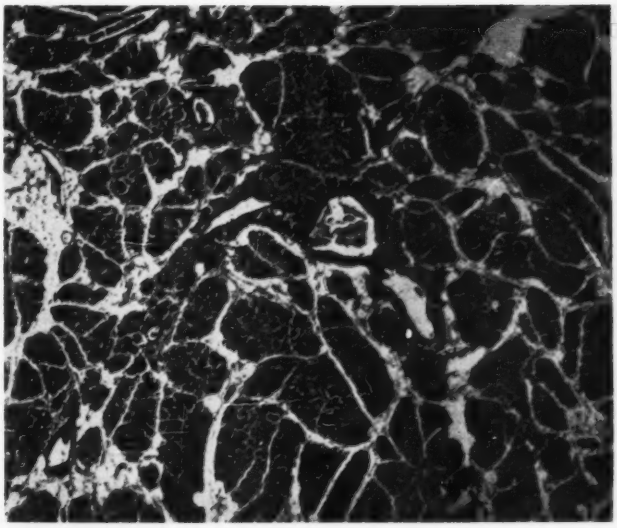

Fig. 9.—Mammary gland of pregnant guinea pig.

managed to say something about the work of my clinic. I shall continue.

People have poked a great deal of fun at us because of the great amount of work that we have carried out on the nipples of guinea pigs, work which has been in progress since 1937 and which we have no intention of stopping. I have already spoken to you about this today. In 1943 Mr. Scherer, a student at our university, asked me for a subject for a thesis, and I advised him to apply estrogens to the nipple of the guinea pig and to examine the mammary gland. He applied a drop of estrogen solution every day for a month to the nipple of the male guinea pig, and he succeeded in evoking a mammary gland resembling completely that of the pregnant female (Figs. 9 and 10). By choosing an appropriate dose, he succeeded in evoking such a mammary gland

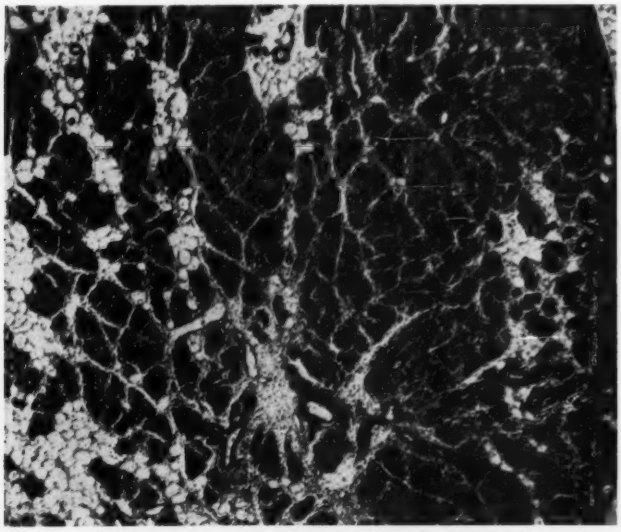

Fig. 10.—Mammary gland of male guinea pig treated by local estrogen application.

only on the side treated. On the other side, the mammary gland did not develop. These experiments carried out on male guinea pigs showed clearly that estrogen evokes the development of the mammary gland in guinea pigs without the intervention of progesterone and without the contribution from the hypophysis. An injection of colchicine given to guinea pigs with a mammary gland in the process of developing resulted in a considerable number of mitoses—what we called a positive Dustin reaction. As far back as 1942, in the *Journal of Investigative Dermatology*, we had already described Dustin reactions in a nipple treated by estrogen.

In a next step we used a nipple treated with estrogens as a test organ for the purpose of examining the effect of x-rays on mitoses, and we found a number of facts which seemed to us not without theoretical interest. I do not press this point; I only want to say that with 400 r we can prevent the mitotic surge not only in the nipple but, according to the experiments of my collaborator Golay, also in the mammary gland.

I shall spare you an account of the many other results that we obtained in using x-rays on the nipple and the mammary gland of the guinea pig. We were very interested in these experiments, always awaiting the results impatiently, although we often told ourselves that it was Art for Art's sake and very far from practical dermatology. But one day we had an idea. The mammary gland, with its numerous mitoses, is an ideal test organ for checking certain new principles of dermatological radiation therapy and radiation effects. Nowadays we want to treat dermatoses with rays which act only superficially, avoiding deep penetration as much as possible. The mammary gland of the guinea pig extends about from 1.5 to 3.5 mm. below the surface of the skin; it is at precisely this depth that we find many of the human dermatoses that we want to treat with x-rays. Originally, in order to find out the physical conditions in which superficial structures could be treated by x-rays without affecting the underlying tissues, measurements were carried out with use of artificial substances as "phantoms" in place of the living tissues. The results obtained in this manner were confirmed by our experiments on the mammary gland. We succeeded in stopping, or not stopping, the mitotic surge in the mammary gland with the same dose by variations in the factors of kilovoltage and filtration (Figs. 11 and 12).

It is evident that the subject that I once gave to a young colleague for his doctor's thesis was entirely and purely theoretical. And we got some results; we did not forget

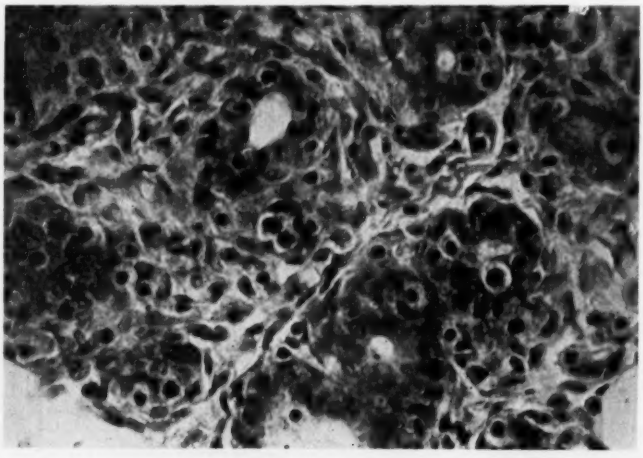

Fig. 11.—Guinea pig mammary gland treated with 400 r, 29 kv.; filter, 0.3 mm. Al. Many mitoses after colchicine injection (Dustin reaction).

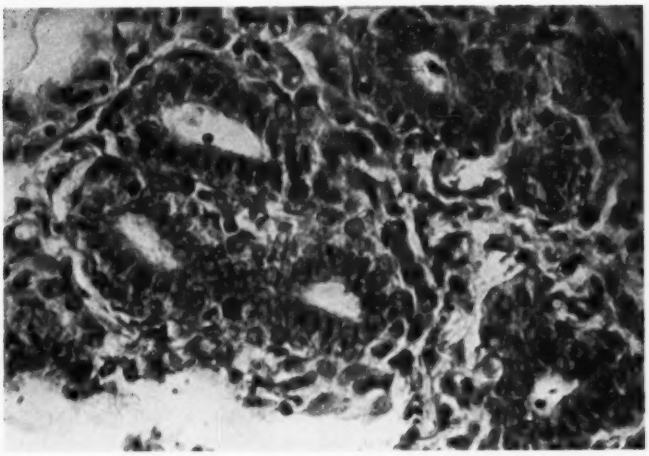

Fig. 12.—Guinea pig mammary gland treated with 400 r, 43 kv.; filter, 0.6 mm. Al. No mitoses after colchicine injection (Dustin reaction).

them but put them aside. Then I asked Dr. Golay to see if he could find any mitoses in the developing mammary gland. Once again it was Art for Art's sake. And finally we have, I think, been able to show that this mammary gland, with its extensive mitoses, is a good test organ for the investigation of dermatologic radiation therapy and its penetration, and we may hope that one day this will have a practical importance.

These examples that I have just given you, and which I offer you under the title "Experiments on Pigmentation and Perspiration, and the Effects of X-rays on the Mammary Gland," must for the moment suffice. I could give you many others.

I shall now tell you briefly about the functions of a director of a dermatologic university clinic and of a professor of dermatology; later, on the basis of all these lengthy expositions, I shall conclude by discussing the question mark after the motto or slogan "Art for Art's Sake? Science for Science's Sake?"

A professor of dermatology in Switzerland has a variety of jobs: *salus aegroti suprema lex*. His first function is to run his inpatient and his outpatient departments. His associates treat the patients, but it is the chief who has the over-all responsibility. He must see all his bedpatients twice a week, more often if anything goes wrong, and every day he must see some of the outpatients. In fulfilling these functions he is always in contact with his assistants, who are nearly all young persons and "full time." The greater number will become dermatologists, while others want to obtain a wider dermatological knowledge for their later general medical practice. Besides being director of a hospital for skin diseases, he also has undergraduate medical students to teach—three hours of clinical demonstrations a week during the entire academic year. In addition, the professor must earn his living. His salary as professor is too little to live on, but it is just too big for him to die of hunger. He is, therefore, obliged to have another office, where he can see private patients. And, on top of all this, the professor and his collaborators, among whom there is a full-time chemist, have the responsibility of carrying out scientific work.

If you compare the life of a professor of a theoretical or "basic science" branch of medicine with that of a professor in a clinical specialty, you find that the former has to give lectures—more, it is true, than a professor of dermatology has to—but what remains of his time he can give to his scientific work. He is, therefore, a privileged person compared with the clinician. But the professor in clinical

medicine has the great advantage that his patients provide him day after day with subjects for investigation. By investigation I do not mean something leading up to a paper entitled "A Case of This or That . . .," or "A Review Concerning This or That . . .," or even "Theories Concerning This or That . . ."; I mean rather work which brings to light some small new fact. My father used to say that one real brick is worth more than a whole building which is no more than a beautiful plan on paper.

The choice of subject of investigation is very important. Why not let the subject be suggested by the illness itself as presented by the patients? Why choose at the outset a subject where practical results are improbable; why not take advantage of the fact that we are running at one and the same time a clinic and hospital and a scientific laboratory? Why should we go in for *pure* science? Is it because it is more noble, because Goethe and Schiller and many others are in favor of pure science? Why not carry out experiments suggested to us by clinical activity, by patients and by diseases, but in the course of our work never neglecting those results which at the time may have only a purely theoretical importance? If we have already chosen a purely theoretical subject, why should we not stop at each result and ask ourselves whether it may have some practical value?

If a colleague carries out scientific work and he finds out something new, he does not want, he does not dare, keep it to himself. He cannot, as he once used to, be satisfied with writing a letter to one of his friends. He must publish what he has found, and publish it in such a way that future research workers can base their work on his results.

We must, therefore, have periodicals and archives. And we must have editors who can carry out the difficult and thankless and unpleasant work of separating the wheat from the chaff and maintaining the standard of their journal which makes so much easier the work of future research workers. It is to the great credit of my father, if you will forgive my saying so, that he edited the *Archiv für Dermatologie*, and it is one of the great credits of Howard Fox that among his many fruitful activities he edited the magnificent American *Archives of Dermatology and Syphilology* that every dermatologist the whole world over must consult if he wants to be up to date or wants to carry out any scientific work. It was also to the great credit of Marion Sulzberger that he founded and for a long time edited the *Journal of Investigative Derma-*

Fig. 13.—Geneva, waiting for the dermatologists of the United States.

*tology* and the famous "Year Book of Dermatology and Syphilology."

After all that I have just said, do you not agree with me in coming to this conclusion: Insofar as medicine is both an art and a science, Art for Art's Sake? No! Science for Science's Sake? No! But art and science both for the benefit of our patients. But let us not forget that it is not often possible to foresee whether the experiments will lead to a practical result or only to one of theoretical interest. We must not neglect any purely theoretical results, because one day they may have the very greatest practical value.

Before sitting down, I should like once more to express my profound respect for the work of the late Howard Fox and my great admiration for American dermatology and also to express my deep appreciation to all those who have invited me. I should like to finish by showing you a photograph, a photograph of Geneva (Fig. 13); while you are looking at it, I should like to tell you how much my wife and I will be delighted if you can come and visit us in our town and in our Dermatologic Hospital and Clinic.

University of Geneva.

# The Association of Psoriasis with Blood Groups

G. K. HARGREAVES, M.B., Ch.B., and F. F. HELLIER, M.A., M.D., F.R.C.P., Leeds, England

The idea that blood groups may be associated with particular kinds of disease is not new, but interest in it has recently been rearoused by statistically significant reports of such associations. The most striking finding is the relatively high frequency of blood Group O in patients with duodenal ulcer, but a number of others have been recorded (Lancet, 1958). We felt it might be useful to see whether any such association could be found in skin diseases, and we selected psoriasis because of its clear-cut entity and its hereditary tendency.

Previous investigations have shown marked disagreement. Klövekorn and Simon (1927) found no correlation between blood groups and psoriasis and also other skin diseases. Nardelli (1928) on the basis of 42 patients came to the same conclusion, though his figures do suggest some preponderance of Group O compared with the normal population. Poehlmann (1928) also found a relative increase in Group O among 268 cases of psoriasis. His figures were as follows:

| | O | A | B | AB |
|---|---|---|---|---|
| Psoriatics, % | 57.46 | 27.99 | 11.57 | 2.98 |
| Normals, % | 41.51 | 42.26 | 10.15 | 6.06 |

Touraine (1942) emphasized this tendency, basing his opinion apparently on the above findings. More recently, Dorn (1956) investigated 200 psoriatics in Germany and found that the distribution of their blood groups corresponded very closely with that of the normal population. His figures were as follows:

| | O | A | B | AB |
|---|---|---|---|---|
| Psoriatics, % | 40.00 | 42.00 | 12.5 | 5.5 |
| Normals, % | 40 | 40 | 15 | 5.0 |

We examined the blood groups of 200 patients with psoriasis and compared them with a large control series from the same geographical area reported by Aird (1953). We obtained the following results:

| | O | A | B | AB |
|---|---|---|---|---|
| Psoriatics, No. (%) | 98 (49) | 81 (40.5) | 18 (9) | 3 (1.5) |
| Normals, No. (%) | 983 (47.6) | 851 (41.5) | 161 (7.8) | 61 (3) |

These findings present a striking similarity between the blood groups in psoriatic patients and normals and show clearly that there is no significant association between psoriasis and any specific blood group.

How can one explain those reports such as Poehlmann's which are at variance with the above? It seems unlikely that an association with Group O occurs in Germany but not in Britain; moreover, Dorn's findings were against this. It might be that their control series were not selected from exactly the same material, for the incidence of blood groups can vary even between places close to each other. Another possibility is that psoriasis may be more frequent in a certain type or strain of person, for instance, perhaps in blonds, and that this type of person also independently shows a preponderance of Group O. Thus the distribution of blood groups in psoriasis would vary from that of a control group of the whole population but might correspond exactly to a control group of the special type.

## Conclusion

There is no significant association between psoriasis and any particular blood group.

20 Clarendon Rd., (2).

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# Carcinoma of Apocrine Glands

*Report of Case*

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Reports on apocrine gland carcinoma are very scant in the literature. This fact can be attributed mainly to three factors. Firstly, the apocrine type of sweat gland is normally distributed in only a few areas of the body and the glands are few in number. Secondly, while benign tumors of the apocrine glands are not too uncommon, the malignant variety is rather rare, and, thirdly, they are not always recognized as such. It is for this latter reason that we feel any addition to the few reports on these rare tumors is valuable.

It is apparent from the literature that even today there is great confusion concerning the true origin of these tumors, and they are put together into one basket under the heading Tumors of Sweat Glands. This procedure is neither justifiable nor very scientific. The tendency should be to separate, whenever possible, sweat gland tumors of the eccrine and the apocrine type. Not only do they differ from one another in origin, but their histology, staining properties, distribution, and the type of secretion are entirely different, and, consequently, it should be always possible to make the distinction morphologically. Since the tumors of apocrine glands are usually slow-growing and anaplasia occurs late, these traits should be helpful in trying to define the type of cells. It is for the reasons mentioned that we feel that another correction in nomenclature should be introduced into the field of the sweat gland tumors; namely, if the prefix "hidro" is reserved for lesions arising in the apocrine glands (i. e., hidradenitis suppurativa, hidradenoma papilliferum), then the term hidrocystoma should be replaced by another one, since this lesion is considered by all authors to be of eccrine gland origin (either glandular or ductal).

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## Histology of Apocrine Glands

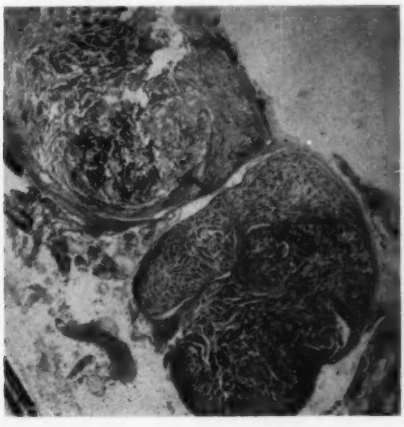
The apocrine glands originate together with sebaceous glands and hair matrix from the primary epithelial germ, whereas the eccrine sweat glands originate from the eccrine sweat gland germ. It is, therefore, understandable that the ducts of the apocrine glands lead into pilosebaceous follicles and not directly to the epidermis. The primary epithelial germ and the eccrine sweat gland germ differentiate from the embryonal stratum germinativum, the former appearing at the end of the first trimester and the latter appearing at the end of the second trimester of fetal life. Except for a few areas where they persist throughout life, namely, in the perianal and perigenital areas, around the nipples, in the axillae, and occasionally over the abdomen and the chest, the apocrine glands involute before reaching their full development. Some authors consider the ceruminous glands of the external ear, the Moll glands of the eyelids, and the mammary glands to be modified apocrine glands.[1]

The name "apocrine" was given to these glands by Schiefferdecker[2] since they secrete by decapitation—i. e., a part of the cytoplasm of the glandular cells is pushed off into the glandular lumen—"apo" meaning off. The lumen of the apocrine gland is approximately 10 times larger than that of the eccrine gland. According to Lever,[1] "the secretory portion has only one distinct

layer of epithelial cells because the outer layer has become differentiated, just as in the sweat glands (eccrine), into myo-epithelial cells. The secretory cells vary greatly in height, depending on the stage of their secretory cycle. The duct is lined by two layers of epithelial cells." Both the secretory and ductal cells are large and have an abundant, deeply eosinophilic cytoplasm, in contradistinction to the cells of eccrine glands, which are faintly eosinophilic, their ductal cells being faintly basophilic. The nucleus is large, round to slightly oval, and situated at the basal third of the cell. The cells contain granules which give a positive reaction for iron.[5] The iron-positive pigment in apocrine glands is of uncertain origin.[6] No such iron-positive pigment is known to occur in eccrine glands. The secretion of the apocrine glands is faintly eosinophilic and gives positive reaction for glycogen when stained with Best's carmine and the PAS technique.

In summary, then it should be easy to determine whether or not a tumor originates from apocrine glands if one considers (1) the site of growth, (2) strongly eosinophilic cytoplasm of cells secreting by means of decapitation, and (3) the presence of iron-positive intracellular pigment. It is possible to recognize these tumors on a histologic basis in spite of their malignancy, because they grow slowly and dedifferentiate rather late.

Fig. 1.—Recurrent tumor. Nodular arrangement of the tumor and incomplete fibrous capsule. Hematoxylin-phloxine-saffron; × 6.7.



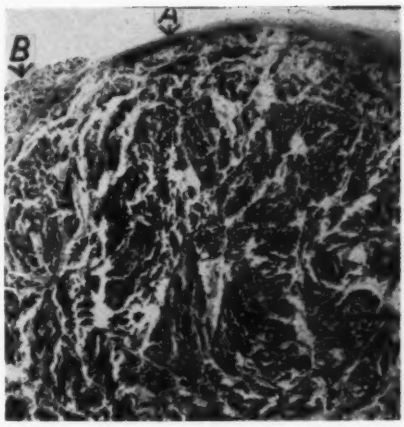



Fig. 2.—Recurrent tumor. Higher magnification of Figure 1, showing penetration of the connective tissue capsule by tumor (*B*) and the cord- and clump-like pattern of cell growth. Hematoxylin-phloxine-saffron; × 27.

## Report of Case

*Clinical Summary.*—A 28-year-old white man, a patient of the Smiths Falls Ontario Hospital, was admitted to Kingston General Hospital on Jan. 6, 1957, for the first time for x-ray therapy to be applied to an area in the left axilla. Four weeks prior to this admission, a tumor mass was removed from the area elsewhere. On admission and during the 15-day stay at the hospital the patient had no complaints. Questioned about the duration of the tumor prior to its excision, the patient said "it was there for some time" and was not able to give any detailed information. He received 300 r units per day for 15 days to the area of excision. Neither on admission nor on his discharge was there any mass palpable in the axilla nor was there enlargement of any group of lymph nodes. On his second admission, in July, 1957, eight months after the removal of the primary tumor, he maintained that the nodular mass reappeared below the original site two weeks prior to admission. On examination, a tumor was found to be situated approximately 2 in. below the anterior fold of the axilla, on the medial aspect of the arm. The skin over it was freely movable. There was no ulceration of the overlying skin. The tumor was removed with use of local anesthesia on July 17. It was well circumscribed, bluish, and encapsulated and was attached by its capsule to the fascia over the biceps muscle. It appeared to be

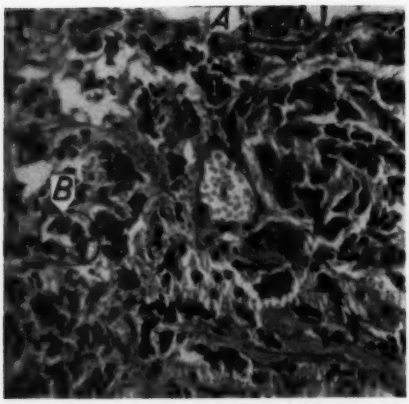



Figure 3

Fig. 3.—Recurrent tumor. In some areas there are small papillary projections (*A*) and an attempt to form glandular spaces (*B*). Best's carmine-Lillit's hemalum-metanil yellow; × 184.

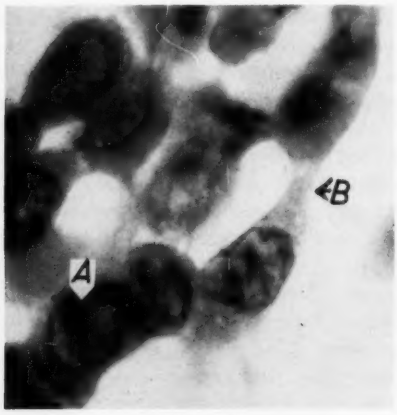



Figure 4

Fig. 4.—Cellular details of the tumor. Secreting cytoplasm is seen in light gray (deeply eosinophilic on section), and the "decapitating" reticular cytoplasmic processes are in continuity with those of the neighboring cells (*B*). The nuclei are large and oval-to-round, with prominent nucleoli (*A*). Hematoxylin-phloxine-saffron; × 1015.

cystic and lobulated. It measured 2 cm. in diameter and 1 cm. in thickness and weighed 2 gm.

*Microscopic Examination of Tumor.*—Microscopic examination showed that the tumor was composed of several round to oval "nodules" (Fig. 1) covered and separated from one another by an incomplete fibrous capsule (Fig. 2, *A*) from which scant connective tissue trabeculae were growing into the substance of the tumor proper. The latter was composed of numerous large cells growing in sheets and cords (Fig. 2), and only very occasionally one could see an attempt at small papillary

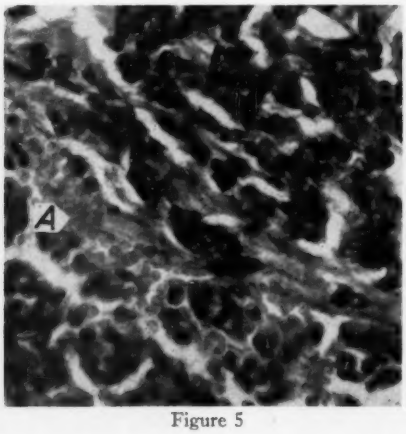



Figure 5

Fig. 5.—Secreting tumor cells in the upper half of the photomicrograph. The PAS material (dark grayish-to-black in photograph, deeply red-violet in the slide) is seen in the cytoplasm in continuity with the intercellular secretion. The cells in the lower half of the photomicrograph are quiescent, nonsecreting. Red blood cells (*A*) are separating the secreting and nonsecreting cells. PAS-Alcian blue-orange G; × 307.

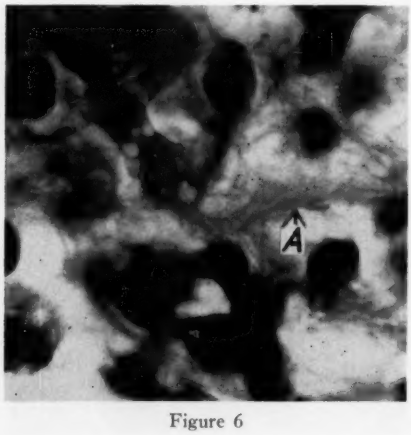



Figure 6

Fig. 6.—High magnification of Figure 5. The cells are seen producing delicate PAS-positive (black in photograph, purple in section) fibrillar material (*A*) extending into the cellular substance and intermingling with similar material of the neighboring cells. PAS-Alcian blue-orange G; × 973.

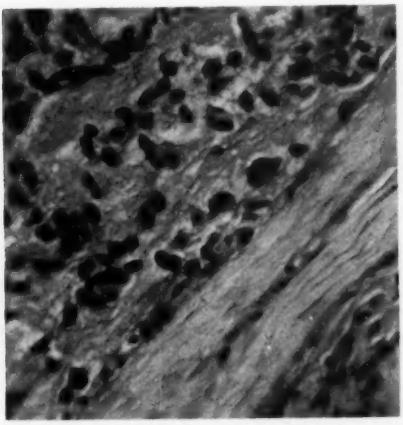


Fig. 7.—Original tumor. The secreted, intercellular material (gray in photograph, reddish-pink in slide) stains positive with mucicarmine. Best's mucicarmine-Lillie's hemalum-metanil yellow; × 307.

(Fig. 3, *A*) or glandular (Fig. 3, *B*) formation. The cytoplasm of these cells was moderately abundant and strongly eosinophilic (Fig. 4). The nucleus was large, oval to round, and plump and stained very deeply. At times a prominent nucleolus was discernible (Fig. 4, *A*). Mitotic figures were moderately numerous. The cytoplasm was seen to be well delineated in some areas; in others, it showed processes (Fig. 4, *B*) which often were vacuolated or reticular, creating the definite impression of secretory activity of the cells. This impression was corroborated by the fact that these cytoplasmic processes were seen in continuity with the secretory material (Figs. 5, 6), which was abundant and constituted the matrix in which the above-described cells were embedded. The secretory material was slightly PAS-positive (Fig. 6, *A*) and stained moderately with mucicarmine (Fig. 7). In areas where the cells were well preserved they resembled strikingly the normal cells of apocrine gland type (Fig. 8). When stained with ferrocyanide, the tumor cells (Fig. 9) contained granules of iron-positive pigment. In some areas these granules were present in a finely dispersed form; in others, they were more or less aggregated.

The microscopic appearance of the recurrent lesion differed in several respects from that of the original tumor.* While the original tumor (Fig. 10) was well surrounded by a thick fibrous capsule (*A*) and the supporting connective tissue was abundant (*B*), on the whole, the capsule of the recurrent tumor (Fig. 2) was thinned out (*A*) and was completely penetrated by the tumor cells in some areas (*B*). Different also was the pattern of growth as well as the degree of cellularity. The tumor grew originally in a predominantly papillary (Fig. 11, *A*) form, producing abundant secretion (*B*), thus resulting in cyst formation, and so the cellular component was rather in the background, the dominating features being secretion, cyst formation, and large amounts of supporting, mature connective tissue elements. The recurrent tumor, on the other hand, showed very little supporting connective tissue and only slight amounts of secretion, and the dominating feature was the

* Dr. J. B. McKay, Central Laboratory, Department of Health, Toronto, supplied us with the tissue of the original tumor as well as valuable information.

Fig. 8.—Normal apocrine gland. The cells are seen to secrete by "decapitation." Hematoxylin-phloxine-saffron; × 410.

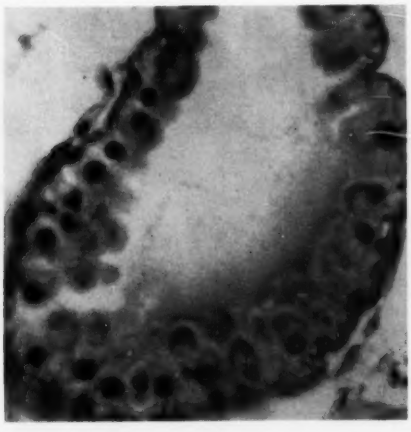
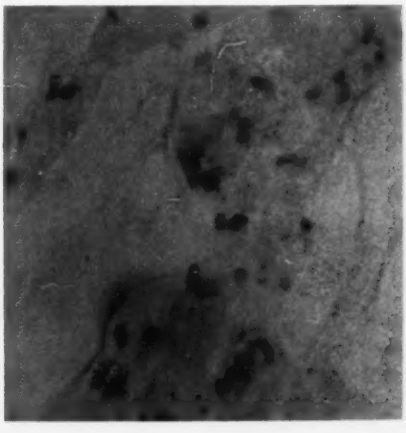


Fig. 9.—Tumor cells containing iron-positive pigment (black in photomicrograph, blue in section). Ferrocyanide-phloxine; × 1015.



extreme cellularity (Fig. 2) with numerous mitotic figures (Fig. 12, *A*). The morphology of the cells and the quality of secretion was the same in both the original and the recurrent tumors.

A radical dissection of the left axilla performed five days later revealed the presence of several large firm lymph nodes at the base of the axilla, being adherent to the latissimus dorsi. Microscopic examination of the lymph nodes showed no tumor cells.

## Comment

In a recent publication [7] Stout and Cooley have reported their own series of sweat gland carcinomas, including only tumors which either metastasized or recurred locally. According to their criteria, our case is justifiably considered to be a malignant tumor, although—on morphological basis—of low-grade malignancy only. The majority of the reported cases [7-9] had been present for some time in an apparently quiescent form before infiltrating or showing metastatic lesions.

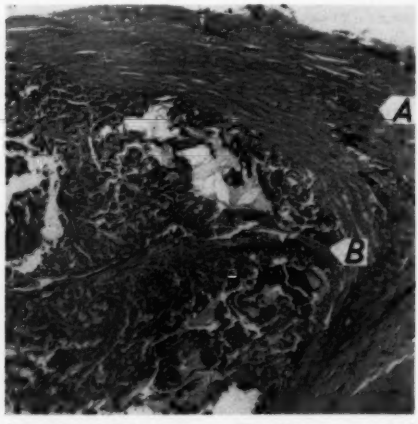


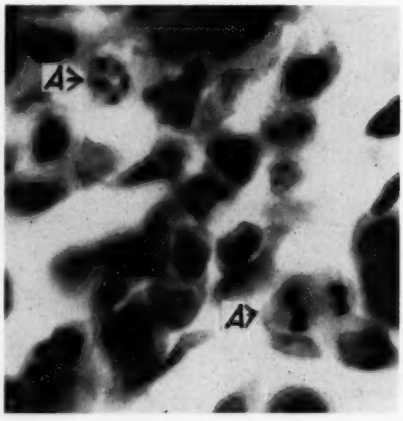

Fig. 10.—Original tumor. The fibrous capsule is thick (*A*), and the supporting connective tissue is abundant (*B*). PAS-Alcian blue-orange G; ×27.

Very little mention is found in the literature about the origin of the malignant variant of these tumors. Are they arising spontaneously as a malignant form in the apocrine glands where the latter occur normally? Or do they take departure from glands which occur in unusual areas? Or

Fig. 11.—Original tumor. The pattern of growth is predominantly papillary (*A*), and the secretion is abundant (*B*). Pentachrome II (elastica omitted); ×27.

is their precursor a benign tumor of apocrine glands such as hidradenoma papilliferum or syringocystadenoma papilliferum? The reports in the literature on this subject are very scanty, as mentioned above.[10] Lever [1] maintains that no malignant variety of the hidradenoma papilliferum or syringocystadenoma papilliferum is known. It would appear, from the morphological studies of the case being reported, that the tumor took its origin in a benign form, namely, hidradenoma, since the originally removed tissue possessed features of this

Fig. 12.—Recurrent tumor. Numerous mitotic figures (*A*). Hematoxylin-phloxine-saffron; ×973.



benign variety. In spite of the well-differentiated appearance of the primary tumor and its apparent perfect encapsulation, the recurrence took place only eight months later. The recurrent tumor showed evidence of malignancy as evidenced by capsular infiltration, increased cellularity with less differentiation and organization, numerous mitotic figures, and an occasional atypical mitotic figure. This tumor was more rapidly growing than the original one.

## Summary

A case of recurrent tumor of apocrine glands is reported to suggest the necessity of separation of this type of malignant tumor from those arising in the eccrine type of sweat gland.

Dr. More, Professor of Pathology, read the manuscript and gave helpful criticism; Miss Nancy A. Hartman gave technical assistance, Mr. Philip Mott took the photomicrographs.

Department of Pathology, Queen's University.

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# Atypical Features in Familial Benign Chronic Pemphigus

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As the clinical concept and histologic specificity of familial benign chronic pemphigus have gradually become widely accepted, this disease entity has been recognized with increased frequency. Over 110 confirmed cases have appeared in the literature since the original description by Hailey and Hailey in 1939.[1] Our interest in writing this report was stimulated by the recent finding of six atypical cases of familial benign chronic pemphigus. It is our purpose to call attention to the unusual features of these cases.

During the process of academic recognition and acceptance, familial benign chronic pemphigus has received a variety of descriptive names, such as chronic recurrent acantholysis (Pinkus and Epstein),[2] vesicular Darier's disease (Ellis),[3] recurrent herpetiform dermatitis repens (Ayres and Anderson),[4] dyskeratosis bullosa hereditaria (Becker and Obermayer),[5] and dyskeratoid dermatosis (Frank and Rein).[6] There is agreement, however, as to the classical features, and these will be outlined briefly.

The lesions begin as small vesicles which soon become flaccid bullae. These later rupture to form amber-colored crusts. A positive Nikolsky's sign is not unusual. The peripheral spread is usually circinate. Most cases appear in early adult life and follow a chronic course with frequent recurrences and varying periods of remission. Sites of predilection include the nape and sides of the neck, the back, the axillae, the inframammary area, and the genitocrural and perianal region. In later life the severity and frequency of attacks subside.[7]

Histologically, the vesicle or lacuna results from acantholysis just above the basal layer. Elevated papillae, lined by a single layer of basal cells, protrude upward into the bullae, and, in some cases, cords of cells proliferate downward into the dermis. Individual prickle cells at the floor of the vesicle may superficially resemble corps ronds; however, the corps ronds of Darier's disease occur predominantly in the granular-cell layers.

There are still those who consider this syndrome, as described by Hailey and Hailey, to be a bullous variant of Darier's disease. Clinically, however, there is a pronounced difference in the appearance of the two diseases, and most dermatologists prefer to think of them as separate entities. Pinkus [2] states that familial benign chronic pemphigus is chronic and recurrent, rather than progressive as in Darier's disease, and that, in spite of many years' duration, the changes remain superficial and flat, without the vegetating lesions so characteristic of keratosis follicularis.

Certainly, the more typical cases are being diagnosed with little difficulty; however, proper recognition of atypical varieties necessitates familiarity with the unusual manifestations of this disease entity. In discussing the differential diagnosis, Popper [8] mentions dermatitis herpetiformis, epidermolysis bullosa, Darier's disease, dermatitis repens, and herpes simplex. The following six interesting cases demonstrate some of the atypical variations which may be found in familial benign chronic pemphigus.

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From the Department of Dermatology, Baylor University College of Medicine (Everett R. Seale, M.D., Chairman), and the Section of Dermatology, Veterans' Administration Hospital.

Fig. 1.—Unusual verrucous lesions and edema of the lower legs in Case 1.

Fig. 2.—Typical lesions of familial benign chronic pemphigus in the groins of Case 1.

## Summaries of Cases

CASE 1.—A 55-year-old Negro man was seen in August, 1955, with a nine-month history of rather severe swelling of the lower legs. About a month previously, he began to develop pruritic vesicles on the extensor surface of the left lower leg. At the same time he developed macerated lesions in the popliteal fossae, groins, and axillae. Shortly thereafter, he developed papular and vesicular lesions over both lower legs.

Physical examination revealed a firm edema of the lower extremities associated with lymphangitic streaking, diffuse erythema, and increased warmth. On the extensor surface of both lower legs were elevated, hyperkeratotic, verrucous lesions (Fig. 1). The neck, axillae, popliteal fossae, groins, and

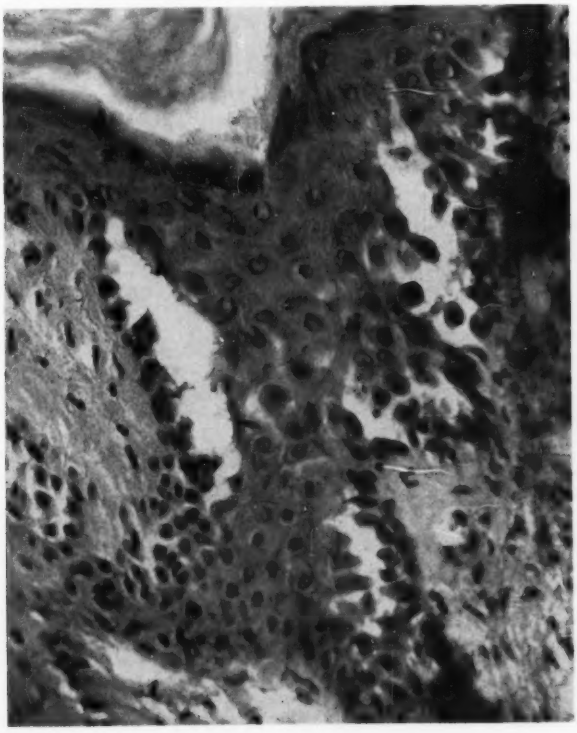


Fig. 3.—Photomicrograph showing the histopathologic findings in a section from one of the verrucous lesions of the left leg.

Fig. 4 (Case 2).—Familial benign chronic pemphigus lesions limited to the vulva of a pregnant woman.

sacral area showed scattered vesicles surrounded by whitish, macerated papules and crusts (Fig. 2). On the plantar surface of the right great toe was a bullous lesion measuring approximately 7 mm. in diameter. Increased pigmentation was present in all involved areas. With bed rest and the oral administration of tetracycline and sulfisoxazole, the cellulitis and vesicular lesions subsided; however, the hyperkeratotic, verrucous lesions on the extensor surface of the lower legs remained unchanged. Since his discharge from the hospital, the patient has periodically developed vesicular lesions in the axillae and groins, and the verrucous lesions have persisted.

Skin biopsies from the right axilla, left groin, and a verrucous lesion of the left lower leg (Fig. 3) were compatible with the diagnosis of familial benign chronic pemphigus. Complete blood cell count, serology, and urinalysis were all normal. A KOH preparation and culture were negative for fungi.

CASE 2.—A 22-year-old Negro woman was seen in July, 1955, with an eruption on the vulva of two months' duration. When this mildly pruritic papular dermatosis was first noticed, the patient was six months pregnant. According to the history, the patient's father has a similar eruption, primarily involving the axillae, which appears in the summer and subsides during the [illegible]ter.

Physical examination showed multiple peculiar whitish papules and plaque-like lesions on the labia majora and adjacent crura (Fig. 4). Over the crural areas there were scattered papulovesicular lesions, even though no intact bullae were present.

The papules on the genitalia and adjacent tissue persisted through the termination of a normal pregnancy. On discharge from the obstetric ward, the patient was given vitamin A, 50,000 units t. i. d., and tetracycline ointment. Two months after release from the hospital, the patient returned with

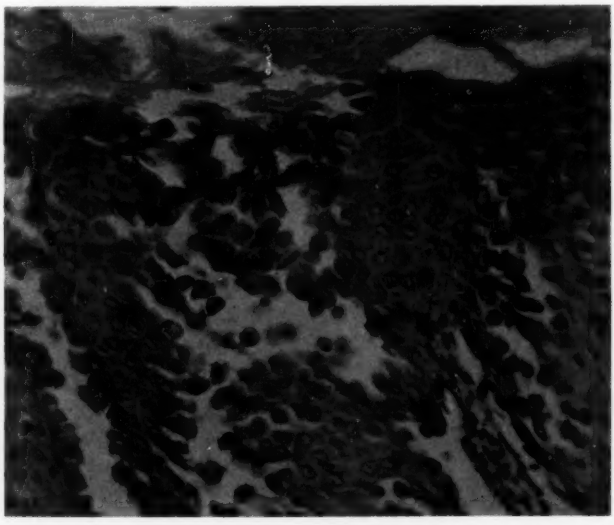


Fig. 5 (Case 2).—Photomicrograph from a vulvar lesion.

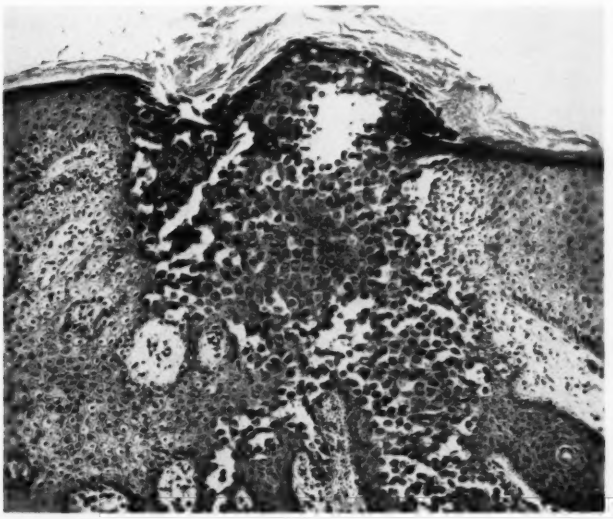


Fig. 6 (Case 3.—Section from a biopsy specimen from a lesion in the axilla.

leukorrhea and erosion of the vulvar lesions. The secondary bacterial infection was treated with systemic sulfisoxazole, hot sitz baths, and a zinc oxide shake lotion containing 0.5% neomycin. As the bacterial infection cleared, the erythematous macerated white papules were again seen. These slowly disappeared, and the patient has remained asymptomatic.

Biopsy of the vulva showed the histologic picture of familial benign chronic pemphigus (Fig. 5). Blood cell counts, serologic tests, and urinalysis were normal. A KOH preparation and culture were negative for fungi.

CASE 3.—A 76-year-old Negro woman was seen in October, 1955, with a severe, painful dermatosis of two months' duration which involved the major part of the hairline along the left frontal, temporal, and parietal areas. Each summer for the past 20 years she has had an eruption involving the axillae. There was no familial history suggestive of a similar dermatosis.

Examination disclosed an acute, weeping, crusting, purulent, pemphigoid eruption over the left frontal, preauricular, and postauricular areas. Flaccid, vesicular, and bullous lesions were present in each axilla. The initial clinical impression was seborrheic dermatitis with a superimposed pyoderma.

The purulent, pemphigoid lesions of the face were treated with saline compresses, penicillin, and sulfisoxazole. The pyoderma subsided, leaving hyperpigmentation and scattered papules that later disappeared without recurrence. The axillary lesions cleared after two weeks of systemic antibiotic therapy; however, they have since shown mild exacerbations.

A biopsy from the left axilla presented the histologic picture of familial benign chronic pemphigus (Fig. 6). The blood cell count, serologic test, and urinalysis were all normal.

CASE 4.—A 55-year-old Negro woman was first seen in July, 1957, with the complaint, intermittent for 13 years, of a pruritic eruption involving the neck, axillae, antecubital fossae, groins, and thighs. This dermatosis began in 1944 with a small vesicle on the side of the neck. Other vesicles developed, and soon both sides of the neck were involved. By 1951, the dermatosis had appeared in the axillae, antecubital fossae, and on the thighs. The disease tended to improve in the fall and to become worse in the summer, with friction and perspiration being aggravating factors. After rupture of the vesicles, the pruritus would be particularly severe. The patient believed that tomatoes,

Fig. 7 (Case 4).—Antecubital lesions clinically suggestive of neurodermatitis disseminata.

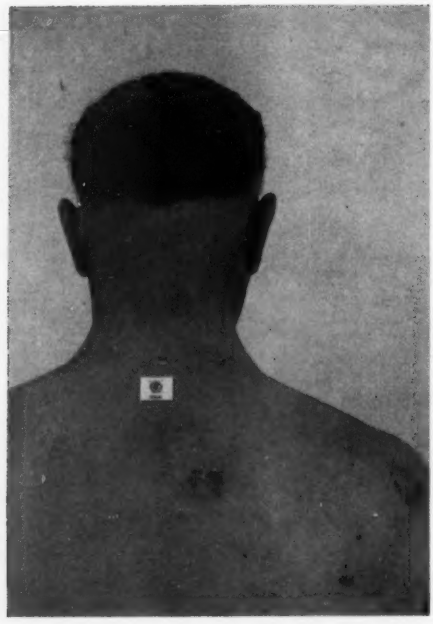


Fig. 8 (Case 5).—Annular lesions on the back and shoulder resembling tinea corporis.

pineapple, milk, beer, and carbonated drinks aggravated her dermatosis. There was no family history of any skin disease.

Examination disclosed weeping, crusting, serpiginous lesions about the neck and axillae. In these sites of involvement there were papules, vesicles, and pustules. The lesions of the antecubital fossae and proximal medial thigh were hyperpigmented, with dry, crusting scales covering an occasional fine vesicle (Fig. 7). These areas manifested excoriations and early lichenification and definitely resembled disseminated neurodermatitis.

Systemic tetracycline therapy yielded some immediate improvement, and with the onset of cooler weather the disease disappeared completely except for some residual scaling and hyperpigmentation.

Biopsies of the neck and arm lesions showed the histologic picture of familial benign chronic pemphigus. The blood cell count, serologic test, and urinalysis were all normal.

Case 5.—A 42-year-old white male office worker was seen in August, 1956, with three annular lesions on the back. He stated that for the last 16 years he has had similar lesions involving the neck, forearms, axillae, and shoulders. The lesions begin as small papules and vesicles which would rupture and leave a weeping, crusted area. Seldom would more than one of the above-mentioned areas be affected at the same time. Excessive sweating, overactivity, or heat seemed to predispose to the development of new lesions; therefore, the disease was usually worse during the summer.

Four years previously, during a period of hospitalization, the patient had been diagnosed by a dermatologist as having a superficial fungus infection. There was no record of a positive KOH preparation or culture. Although the skin lesions improved with topical antifungal medication while he was in the hospital, they became worse after his discharge. There had been no similar disease process among members of the patient's family.

Physical examination revealed a scaling, crusting, erythematous, annular lesion, approximately 3 cm. in diameter, located on the right posterior shoulder (Fig. 8). The border was elevated and active in appearance, whereas the center of the lesion showed clearing. An occasional fine vesicle could be found along the active border. Two additional smaller lesions were present, one to the right in the interscapular area and the other over the right lower scapula. These lesions strongly resembled tinea corporis, and a biopsy was necessary to establish the diagnosis.

With systemic sulfisoxazole and the topical application of a keratolytic solution (resorcinol 2%, salicylic acid 5%, in thimerosal tincture [Merthiolate]), the original lesions on the shoulder and back cleared within three weeks. Two months after discharge from the hospital, new lesions, similar to those described above, developed on the right forearm. The same therapy was effective in clearing them. On follow-up examinations, typical lesions have been seen in the classic areas.

The KOH preparation and a culture for fungi were negative. Biopsy specimens taken from lesions of the right shoulder and arm (Fig. 10) revealed the histologic picture of familial benign chronic pemphigus. The blood cell count, urinalysis, and serologic test were normal.

Fig. 9 (Case 5).—Isolated, circumscribed lesions on the arm, found on another occasion.

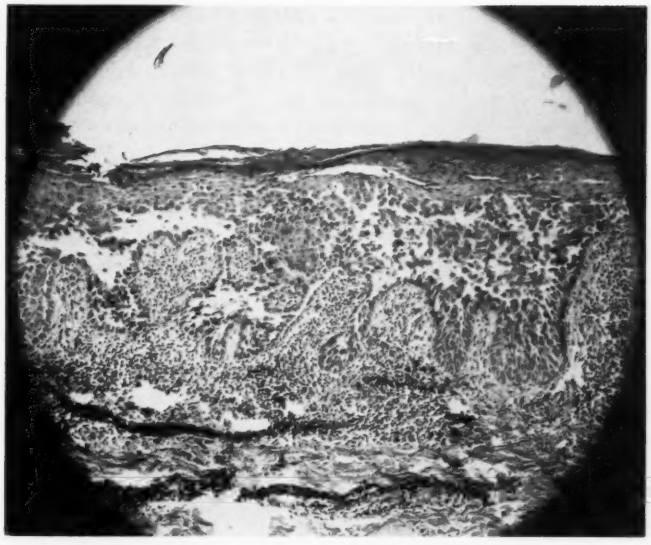


Fig. 10.—Section from an arm lesion shown in Figure 9.

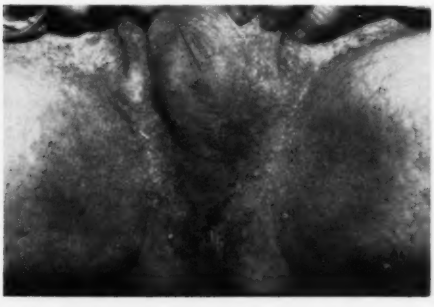
CASE 6.—A 51-year-old white man, a machinist, was seen in July, 1957, with acute inguinal and crural intertrigo. According to the history, the dermatosis had been intermittent for the past 25 years. Exacerbation usually occurred each summer. The neck, axillae, shoulders, upper chest, groins, medial thighs, and scrotum were the areas involved. The disease always began with tiny vesicles which enlarged, ruptured, and left a weeping, crusting, erythematous surface. A few weeks prior to coming under our observation, the man had been treated by a local physician who had prescribed a mercurial lotion. After the use of this medication, the acute crural intertrigo developed. The initial diagnosis was monilial intertrigo with secondary irritation. The patient had a 52-year-old brother who was described as having a similar skin disease.

Acute intertrigo with erythematous weeping surfaces was found to involve the crural folds, medial thighs, and scrotum (Fig. 11). There were annular lesions on the neck and shoulders which were composed of erythematous scaly papules and vesicles. Occasional fine vesicles were seen on adjacent normal skin. In the axillae he had only erythematous papules.

Repeated KOH preparations and cultures from the inguinal lesions were negative. Biopsy of a neck lesion showed the histologic picture of familial benign chronic pemphigus. A blood cell count, serologic test, and urinalysis were all normal.

Cool compresses and hydrocortisone lotion were applied, and the acute inguinal dermatitis subsided. As the dermatitis improved, it continued to resemble a monilial intertrigo. The neck, shoulder, and axillary lesions showed little response to topical hydrocortisone therapy.

Fig. 11 (Case 5).—Lesions of the groin resembling a monilial intertrigo.



## Comment

These six cases of familial benign chronic pemphigus present varied and interesting clinical aspects. In addition to the typical lesions of familial benign chronic pemphigus, Case 1 had hyperkeratotic, verrucous lesions on the lower legs. Such lesions have never before been reported to occur with this disease entity. This case was presented to the dermatology section of the Southern Medical Association and Dr. Hugh Hailey commented that this patient had all of the criteria necessary for the diagnosis of familial benign chronic pemphigus; however, he

raised the question as to whether the verrucous lesions were actually a part of the disease process. A biopsy of one of these revealed the typical intraepidermal bullae of familial benign chronic pemphigus.

The second case, with white-topped papular lesions on the external genitalia, was peculiar in that the disease was apparently precipitated by pregnancy and was localized to the vulva. The eruption disappeared after the elimination of a postpartal leukorrhea. In addition to typical lesions in the axillae, Case 3 presented pemphigoid, vesicopustular lesions involving the left frontal and preauricular hairline. It can be theorized that a pyoderma predisposed to the development of lesions in such an uncommon site, but it is not possible to determine whether the pyoderma was primary or secondary.

Case 4 manifested widespread lesions involving the neck, antecubital fossae, axillae, and thighs. The distribution and clinical appearance of this dermatosis was such that it had been erroneously diagnosed as neurodermatitis disseminata by a capable dermatologist. The fifth patient had lesions with erythematous vesicular borders and clearing in the center which looked like tinea corporis. The last case exhibited lesions of the groin that were originally mistaken for a monilial intertrigo.

Of the six cases reviewed, only two had a familial history of the disease. Four of the six patients gave a history of exacerbation related to hot weather. The routine laboratory data revealed no abnormalities. Two of the patients were white, and four were Negro, despite the fact that the literature indicates that this disease is rarely found in the Negro race.[9] Although various forms of treatment for familial benign chronic pemphigus have been suggested, systemic antibiotic therapy has been reported to be the most satisfactory.[10] The systemic administration of antibiotics was beneficial in five of these six cases.

From the atypical features of the above cases, it can be seen that familial benign chronic pemphigus is a disease syndrome that may be easily confused with other dermatoses. The disease may appear in sites other than the classic areas, and the individual lesions may be unusual in appearance. A biopsy is often required to make the diagnosis.

## Summary

Six atypical cases of familial benign chronic pemphigus are presented and discussed.

Case 1 manifested verrucous lesions on the legs, and such lesions have never been reported to occur in this disease.

In one patient, Case 2, the disease appeared during pregnancy, was localized to the vulva, and disappeared after elimination of a postpartal leukorrhea.

Pustular, pemphigoid lesions of the face and adjacent scalp were found in Case 3.

A clinical picture resembling neurodermatitis disseminata was presented by Case 4.

Case 5 presented lesions resembling tinea corporis, while Case 6 had lesions similar to those found in monilial intertrigo.

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# Lichenoid Eruptions Following Contact Dermatitis

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Lichenoid-type lesions, following contact dermatitis, have been observed in photographic operators who handle certain *p*-phenylenediamines. The subject of lichenoid skin eruptions was recently reviewed from the histopathologic standpoint by Winer and Leeb.[1] No mention was made of lichenoid eruptions following skin contact with allergens.

These aromatic amines are used in making chemical intermediates, dyes for furs, antioxidants for gasoline, antioxidants for rubber, and as color developers in the photographic trade.[2] When used in photography, they have the interesting property of coupling with other chemicals to form a dye image. In this situation, they are partially oxidized to complex substances when exposed to air. Preventive measures observed by the photographic trade following skin contact with these agents are discussed in a final paragraph.

Generally speaking, the cases of contact dermatitis seen in the photographic industry resulting from skin exposure to aromatic amines may be classified into two broad groups: First, there is the acute type, featuring an intense eczematous response but showing in addition, histopathologically, liquefaction of the basal layer. The acute type amounts to less than 10% of the total cases observed. On subsidence of an acute eruption, residual lesions are observed to be lichenoid in type. Second, there is the subacute type, in which the lesions develop slowly and usually appear lichenoid from the beginning. In this latter situation, if the skin contact with the amines is sufficiently great or the time the chemical remains on the skin is prolonged, the subacute process may evolve into the acute variety.

The earliest constant clinical finding noted in sensitized operators who have sustained repeated minor contact of the skin of the fingers with these aromatic amines is loss of eponychial tissue and a reddish-purple discoloration of the distal dorsal phlanges. An inconstant early finding is a petechial eruption occurring on the tips of the fingers. With further exposure, the skin of the interdigital web spaces shows a confluent, violaceous, edematous, papular response (Fig. 1). Additional exposure leads to the development of discrete, violaceous, eczematous and lichenoid lesions on the anterior wrists (Fig. 2), which may shortly thereafter become confluent (Fig. 3). The acute eczematous quality of this eruption points out the fact that the patient's dermatitis has passed into the acute type from the subacute variety. If the operator is not removed from contact with the specific chemical at this stage, there may result a generalization of the eruption. This cutaneous expression is manifested by an extension of the eruption on the arms, by a confluent mildly edematous papular response situated about the skin of the anterior and lateral sides of the neck, and by discrete violaceous papular lesions scattered over the remainder of the body, including the genitalia. The face is ordinarily spared. No oral mucous membrane lesions have been noted in the cases observed to date.

The intensity of the skin reaction varies, therefore, from an essentially dry papular response, the subacute type, to a wet papu-

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lar or eczematous response, the acute type. The reddish-purple or violaceous color is present throughout the acute or subacute skin reaction. Healing progresses, in the case of an intense, acute skin reaction, first by loss of evidence of clinical eczematization. The remaining dry papule is indistinguishable clinically from the papule characteristic of lichen planus (Fig. 4). Histopathologically, the findings may be similar to those of lichen planus[3] (Fig. 5). However, many of the sections studied show in addition a spotty parakeratosis and a more intense perivascular and adnexal infiltrate.

Further healing continues through the pigmentary phase characteristic of an intense lichen planus reaction. Pigmentary changes have not been permanent, but, in dark-complexioned persons, have taken up to a year or more for complete clearing.

In addition to the lesions described, and at any stage of the eruption, some operators may show papulovesicular lesions on the upper forearms, and particularly about the antecubital spaces (Figs. 6 and 7). These lesions are not peculiar to contact with aromatic amines but represent sweat retention and have been previously noted clinically as a primary or secondary dermatosis.

Symptomatically, patients who have lichenoid eruptions following contact dermatitis usually complain of moderate to severe pruritus. This complaint ordinarily subsides rather promptly on removal of the worker from chemical exposure. Workers who have sustained palmar skin reactions usually complain of excessive sweating of the skin of the palms and palmar aspect of the fingers. This may persist for months following subsidence of the dermatitis. With an experience of 25 years' observation, no permanent vascular sequelae have been noted following this intense skin reaction.[4] The majority of the patients are concerned initially by residual pigmentation of the skin following a severe case of dermatitis. Reassurance and explanation that the pigmentation will not persist are important in allaying their concern.

### Laboratory Data

No evidence of systemic involvement associated with contact dermatitis caused by aromatic amines could be determined from complete blood cell counts and urinalysis.

### Histopathology

Biopsy specimens were taken, without anesthesia, with use of the high-speed "Electric Punch." Tissue sections were fixed in 10% formalin and stained with hematoxylin and eosin.

Histopathologic study of the very early subacute lesions shows an intense reaction about the blood vessels in the upper cutis. More fully developed lesions, additionally, show a dense infiltrate consisting chiefly of lymphocytes and polymorphonuclear leukocytes concentrated in the upper cutis and also distributed perivascularly about the vessels of the mid and lower cutis, as well as the adnexal structures in the latter situation. Liquefaction degeneration of the basal layer is noted. With severe acute reactions, spongiosis and vesicle formation are noted as well.

Old lesions show hyperkeratosis with occasional spotty parakeratosis, granulosis, irregular acanthosis, liquefaction of the basal layer, and a heavy infiltrate consisting chiefly of lymphocytes and polymorphonuclear leukocytes situated in the upper cutis and distributed about the vessels of the cutis and adnexae. Occasional mast, plasma, and epithelioid cells are also found in the infiltrate.

### Epidemiology

Initial observation of an isolated case of a lichenoid eruption following contact dermatitis may lead one to consider it as clinical lichen planus, or as having been produced through a Köbner effect. There is probably no question that certain *p*-phenylenediamines might produce a localized lichen planus reaction, when in contact with skin, as will other contact allergens in persons who have, or give a history of having had, clinical lichen planus. However, obvi-

ous features which establish lichenoid eruptions secondary to skin contact with these agents may be summarized as follows:

1. Subsidence and clearing of the lesions follow removal of the worker from further contact with the causative agent.

2. The histopathologic findings of lichenoid eruptions following contact dermatitis evolve distinctively.

3. In a recent personal communication,[5] the incidence of lichenoid eruptions following contact dermatitis in a color photographic processing plant, apparently not observing preventive measures, was stated to be approximately 25%. Contrast this with a recent study[6] of the first 1700 dermatologic cases referred for consultation in a film manufacturing and chemical industry where the incidence of lichen planus was well below 1%.

4. Workers who have developed lichenoid eruptions following contact dermatitis have thus far given no previous history, nor do their medical records show that they have ever had lichen planus.

5. The Köbner effect is ordinarily a localized phenomenon brought about by trauma in persons who usually present other evidence of having had lichen planus, psoriasis, etc., or give a history of having had these diseases.

## Patch-Test Studies

Lichenoid eruptions following contact dermatitis occur only in sensitized persons.[7] The hydrochloride salt of the substituted *p*-phenylenediamines when applied to the skin of a sensitized operator will produce an eruption (Figs. 8 and 9) which evolves to duplicate the lesions seen clinically. The chemical to be applied to the skin is freshly prepared by appropriately diluting it with distilled water to make a 1% solution. Closed-patch technique is most conveniently used. The patch is removed in 24 hours, and the underlying skin is washed gently with an acid-type skin cleaner. This latter procedure serves to remove excess chemical, which, because of its proclivity to become fixed to epidermal cells, might lead to sensitization by the patch test itself.[8] Skin reactions are read at 1 hour and again in 24 and 48 hours after removal of the patch test. Evolution of the lesion over the next few days produces the typical lichenoid eruption.

Ordinarily, skin reactions tend to be specific for each differently substituted *p*-phenylenediamine. On occasion, cross reactions may occur. The brownish stain remaining on the skin after removal of the patch and subsequent washing should not be confused with a positive skin reaction.

## Preventive Measures

The preventive measures[9] employed to control contact dermatitis in the photo-

Fig. 1.—Subacute contact dermatitis. Early findings. Note reaction on distal dorsal phalanges and interdigital web spaces.

Fig. 2.—Subacute contact dermatitis. Note lichenoid quality of the lesions.

Fig. 3.—Acute contact dermatitis. Eruption has become confluent on anterior wrists. Note violaceous color.

Fig. 4.—Subsiding acute contact dermatitis. Note linear arrangement of lesions on dorsal aspect of hand from contact with rack used for holding film. Note lichenoid quality of the eruption.

Fig. 5.—Tissue section taken from eruption on phalanges noted in Figure 4; × 15. Section reveals hyperkeratosis, granulosis, irregular acanthosis, liquefaction of the basal layer, a dense infiltrate consisting chiefly of lymphocytes and polymorphonuclear leukocytes concentrated in the upper cutis and also distributed perivascularly about the vessels of the mid and lower cutis as well as the adnexal structures in the latter situation.

Fig. 6.—Papulovesicular eruption noted particularly about antecubital spaces.

Fig. 7.—Tissue section taken from lesion within the encircled area noted in Figure 6; × 50. Section reveals pink-staining keratinous material in the epidermal portion of a sweat duct. This overlies a circumscribed, dense infiltrate consisting chiefly of lymphocytes and polymorphonuclear leukocytes. Serial sections studied reveal the sweat duct to be pervious in its intradermal portion. Thus, the lesion is consistent with a miliaria profunda.

Fig. 8.—Results of patch test application of three differently substituted *p*-phenylenediamines. Note positive reaction in center. Sites 1 and 3 show brown staining only on skin.

Fig. 9.—Tissue section taken from site of positive patch test shown in Figure 8; × 15. Section removed 48 hours after application. Note intraepidermal vesicle formation, spotty, dense infiltrate in upper cutis with liquefaction of basal layer, and intense perivascular and adnexal infiltrate. Infiltrate consists chiefly of lymphocytes and polymorphonuclear leukocytes.

Figure 1

Figure 2

Figure 3

Figure 4

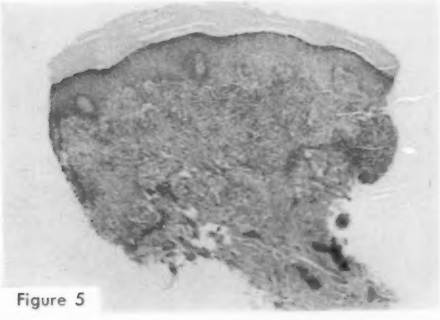

Figure 5

Figure 6

Figure 7

Figure 8

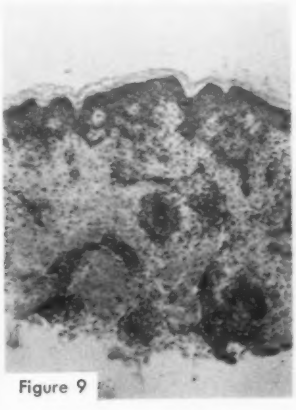

Figure 9

graphic industry may be summarized briefly as follows:

1. Proper selection of operators. Avoid, if possible, operators with chronic skin disorders.

2. Proper training. Care in the handling of these chemicals used in indusry. Good housekeeping in the laboratories and work areas. Moreover, training should be continuous.

3. Avoidance of actual contact with chemicals. Mechanize chemical processing equipment to reduce skin contact. Use rubber gloves and aprons.

4. Removal of the chemical from the skin as soon as possible. Dilution with quantities of water and use of an acid-type skin cleaner.

5. Prompt medical attention to operators who have sustained considerable skin contact with substituted *p*-phenylenediamines.

## Summary

Lichenoid eruptions following contact dermatitis occurring in workers who handle certain *p*-phenylenediamines are discussed from the clinical and histopathologic viewpoint. Certain facts regarding the epidemiology and the specificity of the skin reactions are reported. Preventive measures to be taken by industry and the operator in control of this dermatitis are outlined.

Eastman Kodak Company.

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# Anecdotes of an Agnostic Allergist

WALTER C. LOBITZ Jr., M.D., and OTIS FIELD JILLSON, M.D., Hanover, N. H.

## Introduction

When the members of your program committee bestowed upon me the honor of delivering the William Allen Pusey Lecture this year, I am sure they did this in all good faith. With sincere innocence and honesty they asked me to speak on a topic of my own choosing. Thus, if criticism is warranted, it should be directed toward me rather than the committee. In such a situation as this, one should speak of what one knows. I choose, however, to speak of what I do not know. Thus, instead of this being an address of my knowledge, it will be one of my ignorance.

I am aware that my reputation, such as it is, in our specialty is more that of a basic science investigator than of a clinician. I am, therefore, no doubt unwise in not presenting to you some basic science material. You are probably aware that I am a basic science investigator only one day a week. The remainder of the week I am a physician practicing and teaching the specialty of dermatology. It is as a practicing clinician that I shall address you this evening. I shall say nothing new or original. I shall ask and raise many questions but will give no answers. I shall even be ventilating my frustrations arising out of my own lack of knowledge.

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From the Department of Dermatology, Hitchcock Clinic and Dartmouth Medical School.

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Why this title, "Anecdotes of an Agnostic Allergist"? Anecdote is defined as "a tale" or "an account." Agnostic is of Greek derivation meaning "not knowing" or "unknowing." This is precisely what this address will be—an account of a practicing clinician who is skeptical because he is unknowing in the field of allergy.

One gathers the impression that in general the teaching centers along the Eastern seaboard are more sympathetic to the practical role of allergy in the specialty of dermatology. One also gathers that the Midwestern teaching centers, with exceptions of course, are more sympathetic to the psychosomatic approaches to urticarial and eczematous disease.

I was born, reared, and medically educated in Ohio; married in Oak Park, Ill.; and trained in dermatology in Minnesota. I am happy with the doctrines that were taught me. For the past eleven years I have been in New England, facing, as all of us must in any area of the country, an endless procession of urticarial and eczematous disease. During most of this time I have had the good fortune to be associated with Dr. Otis Field Jillson, born in Maine, medically educated in Boston, and trained in dermatology in Boston and New York, and, incidentally, very knowledgeable about the practical application of the basic rules of allergy to the practice of dermatology. This, then, is an account of our swinging pendulum of dermatoallergy in Hanover, N. H.

There are many known and unknown mechanisms on each side of this pendulum (Fig. 1). If one starts with the urticarial lesion, one can quickly trace it up the allergy side, past "signs," "symptoms," and "morphology," to the release of histamine and/or acetylcholine and/or 5-hydroxy-

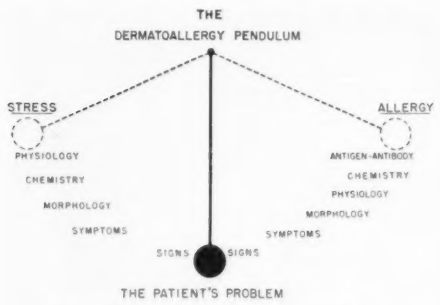


Fig. 1.—The dermatoallergy pendulum.

tryptamine to the antigen-antibody mechanism.

The antibody is called an "atopic reagin," is located in the patient's serum, can be passively transferred with this serum, can be destroyed by heat, and cannot pass the placental barrier. These things we know.

It is just as easy to go up the stress side of the pendulum (Fig. 1), because we can clinically recognize and reproduce cholinogenic urticaria with small wheals and large axon reflex flares that are produced by exercise, heat, and emotions. We know the mechanism by which this occurs (Fig. 2). These physiological stimuli which we associate with flushing, blushing, and sweating are associated with a rise in rectal temperature from 0.2 to 1 F. This increase in blood temperature acts on the heat-regulating center; the cholinergic nerve is then stimulated (and can be blocked by procaine [Novocain]) to release acetylcholine, and maybe histamine, to produce the clinical lesion of cholinogenic urticaria. We also recognize the systemic symptoms that occur from release of acetylcholine in over 50% of the patients with this clinical problem, i. e., sweating, flushing, abdominal cramps, diarrhea, salivation.

In dermatology we seem to prefer to make a diagnosis of chronic urticaria on a functional basis. If we do this, at least the statistics are in our favor. However, are we fair if we deny such a patient a total

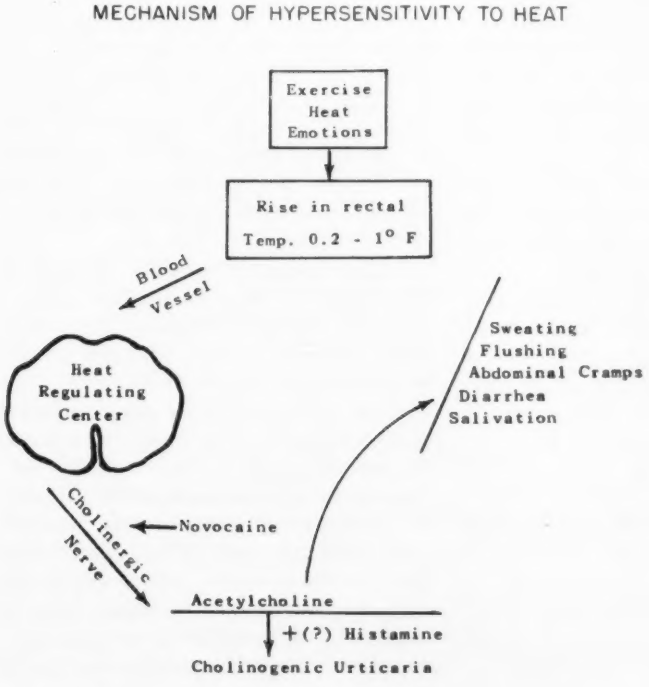


Fig. 2.—The mechanism of hypersensitivity to heat that produces cholinogenic urticaria and in 50% of these patients other systemic manifestations of acetylcholine hypersensitivity.

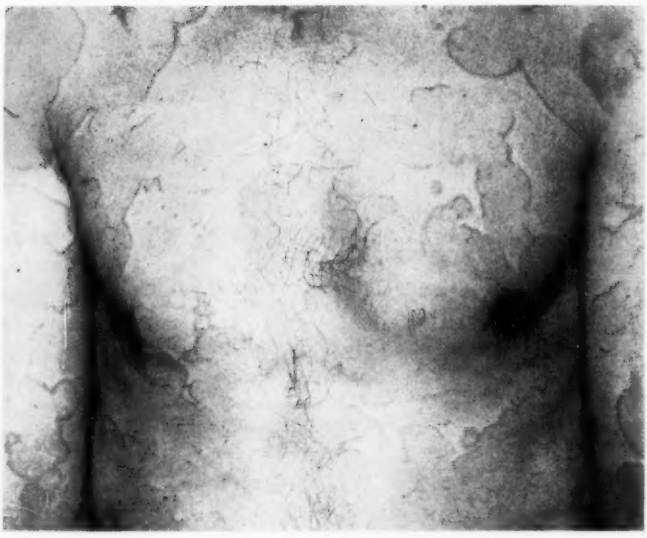

Fig. 3.—Annular urticaria showing central clearing resulting from the development of local tissue anergy; at the same time the advancing border is in the area of hypersensitivity.

evaluation, including a proper allergic survey?

Here is a case in point, one on which I stubbed my toes some years ago. This patient had chronic urticaria for over three years. He and I and a consulting psychiatrist were happy with the emotional etiology of his disease even though we were not curing him. Then he noticed that his hives were gradually developing annular and gyrate patterns (Fig. 3). Of course, it is not unusual for patients with chronic urticaria to develop annular lesions. This time, however, it made me recall some basic rules in allergy that I had learned at one time, perhaps for my "Board Exams," and then apparently had forgotten.

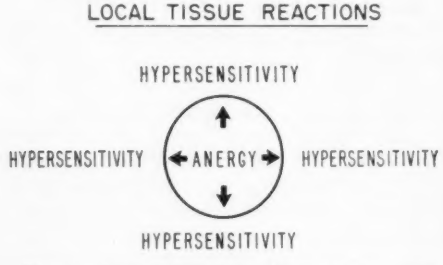


Fig. 4.—Spontaneous local tissue allergic reactions as seen in annular urticaria, erythema annulare centrifugum, etc.

Of course, by definition, we need three key criteria in order to label a condition allergic. It must be acquired, it must be to a specific allergen or cause, and there must be an alteration in the capacity of the tissue to react, in this case to produce a wheal. We all know that the atopic persons who develop chronic hives are notorious reactors to many antigens that produce urticarial lesions. Thus we have come to have little or no faith in the use of immediate-wheal skin tests in this group, because there was no specificity of these tests toward the patient's problem.

I then remembered that the alteration in the capacity to react includes an increase (hypersensitivity), a decrease (hyposensitivity), and an absence (anergy), but always specific to a given antigen.

I can, by rule, transfer these definitions to local tissue reactions (Fig. 4). Whether we are talking about allergic reactions such as hives, or erythema annulare centrifugum, or even about infections such as ringworm of the skin, these annular lesions are known to spread peripherally and clear centrally because they develop a temporary local tissue anergy, or immunity in the case of infection, in the center of the lesion. At the

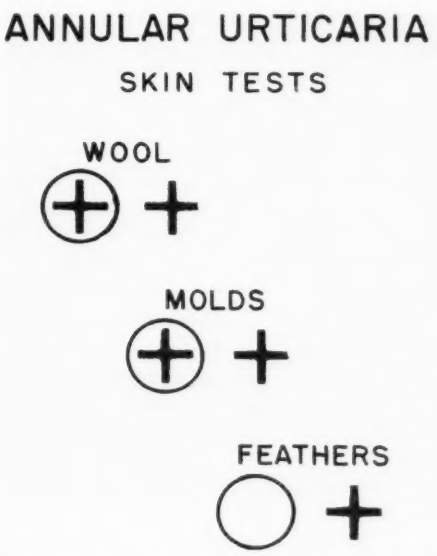


Fig. 5.—Immediate-wheal reactions to intradermal skin tests placed inside and outside of the annular urticarial lesions.

same time, the hypersensitivity remains outside the lesion.

Perhaps if I were to skin test this patient inside and outside of his annular lesion, I might gain some information regarding specificity. In areas that were free of urticaria, I introduced 13 intradermal skin tests that had been selected after an adequate history. The patient developed positive immediate-wheal reactions to three of these: wool, molds, and feathers. He was retested to these antigens both inside and outside of an urticarial wheal (Fig. 5). The wool showed hypersensitivity (a wheal) inside and outside the lesion. Thus, this was not specific to this particular local tissue reaction. The molds showed hypersensitivity both inside and outside the lesion and thus this, too, was not specific. The feathers, however, although demonstrating hypersensitivity outside the lesion, did not react inside the lesion. Hence, a specific local tissue anergy was demonstrated. The specificity resided only with the feather antigen. Avoidance of feathers resulted in cure. We have since utilized this procedure as routine on all similar patients.

Like other agnostic allergists in the audience, I must be skeptical. Maybe my positive approach cured this patient's emotional hives; maybe he solved his emotional problems at the same time that I thought I had cured his allergy. It is certainly very difficult for any one of us to convince any other one of us of anything when it comes to a patient's response. But I wonder if in the practice of clinical medicine we are consistent in our desire for controlled evaluation of treatment responses. If we are prejudiced in favor of a given approach, are we not as clinicians apt to overlook the need for controlled evaluation of our patient's response? Then, again, if we are prejudiced against a given approach, do we not vigorously demand adequate control and proof by our opponents?

Controls in the practice of clinical medicine are difficult, indeed, because the main goal in our offices is to get the patients well. Apparently the problem of control can even be a stumbling block in obtaining scientific information. In this regard, and in a facetious mood, one of the speakers at the recent Research Meeting for Nervous and Mental Disease pointed out the problems in "blind testing." The speaker mentioned that, even though we have at first demanded the "single-blind" study, wherein the patient does not know what he is being given, and even though we then have become more exacting and have demanded the "double-blind" study, wherein neither the patient nor the doctor knows what the patient is being given, he would not be surprised to hear of a "triple-blind" test, wherein neither the patient nor the doctor knows what the patient is being given and neither of them knows what it is for in the first place. Be that as it may, my only "drum-to-beat" is that, if we have more than one approach to the diagnosis and/or treatment of a chronic disease, let us give the patient the benefit of all of our knowledge rather than only a part of it.

But let us come back to the pendulum (Fig. 1) and talk about our greatest plague, eczema. If we swing up the allergy side, we clinically recognize eczema, that it itches acutely and chronically, that the microscopic morphology is that of spongiosis, and that all of this is produced at the cellular level by an antigen-antibody mechanism.

The antibody is located in the lymphocyte and has been passively transferred with the lymphocyte. The reaction of the cell that we call the shock-organ is usually a delayed one in contrast to the immediate urticarial reaction. We recognize this mechanism in contact allergic dermatitis, in so-called "id" reactions such as are seen in Trichophyton infections with hypersensitivity, and in drug eruptions such as one type of penicillin allergy, and unequivocally proven cases have been reported in the literature to be due to the inhalation of wool, ragweed pollen, ingestion of food dyes, etc.[1]

I am a little less smug when I let the pendulum swing up the stress side (Fig. 1). Neurodermatitis in its various forms is the name we attach to chronic, noncontact, eczematous dermatitis, i. e., exudative neurodermatitis and disseminated neurodermatitis; even the term dyshidrotic dermatitis with the sweating palm connotes an emotional etiology. However, unlike emotional urticaria, I have yet to see spongiosis and eczema experimentally produced by stress alone, and if these are thought to be produced by stress, the manner in which this happens has not been explained. To me spongiosis is the most frustrating and yet perhaps one of the most exciting keys to the problem of eczema. How can one produce spongiosis other than by an antigen-antibody mechanism?

I can point out in the literature that experimentally produced allergic eczema in animals and in man is made worse in a frustrated group in comparison with a controlled group.[2] We also heartily agree with the diagnosis of specific defects in the personality pattern of the patients with disseminated neurodermatitis,[3] which when corrected result in less or no eczema. I can even glibly postulate that if a lymphocyte is loaded with an eczematous antibody and if, as is known in times of stress, the lymphocyte is flooded into the system and is then broken down it may presumably free this eczematous antibody into the system and thus produce an allergic neurodermatitis or eczema in this manner. In spite of all this, to my present knowledge spongiosis has not been produced by stress alone, and spongiosis has not been produced in the absence of an antigen-antibody reaction.

In our own department and laboratories we have been trying for 10 years to do just this—to understand and/or to produce eczema without the presence of allergy. Much of the basic work that we have been reporting is all ground work directed toward this goal. At first my confidence in our clinical observations lulled me into false complacency. If it was inter- or intracellular edema of epidermal cells that I wanted to understand, why not start out with something easy, like a thermal burn, even though this was not the true histologic picture of eczematous spongiosis? Then the production of burns by hypnosis was the obvious next step to understand how man's psyche could produce edema in the prickle cells. We worked with our Department of Psychiatry on this. We failed. Success in the production of hypnotic burns has been reported in the literature; careful observations of some of the experiments, however, indicate that the hypnotic suggestion was so strong to the subject that he successfully burned himself once awakened, in order to please his hypnotist.[4] Be that as it may, burns are not true eczematous spongiosis. We gave up this approach.

Dyshidrotic dermatitis surely would give us a clue. Here was true spongiosis with clinical eczematous vesiculation occurring in a sweating palm, and a palm can only be stimulated to sweat by mental or emotional stimuli. We worked on the sweating angle first. We thought we carried out good studies in cutaneous physiology, pharma-

Fig. 6.—Dyshidrotic dermatitis of the hands of 10 years' duration before sympathectomy.

cology, histology, and histochemistry. All we proved was that the vesicles were not sweat-retention vesicles, were not anatomically related to the sweat structure, and could not be produced or altered by acute experiments of this type.

Therefore, we went around the other way. We decided to turn off the sweat over a longer, more chronic, period and observe the effect. Unilateral stellate ganglion blocks seemed to make the patient's hand feel better. We were not convinced. The neurosurgeons then produced for us, in several patients, a unilateral anhidrosis of one hand of 6 to 12 weeks' duration by injecting alcohol into the stellate area. The clinical response of the patients' symptoms, but not the signs, encouraged us to go further.

A patient who had been repeatedly incapacitated with classical dyshidrotic dermatitis of the hands and feet (Fig. 6) for 10

Fig. 7.—Same as Figure 6—close view of the thenar area. Note the hyperhidrosis, minute intraepidermal vesiculation, and secondary cracking and scaling.

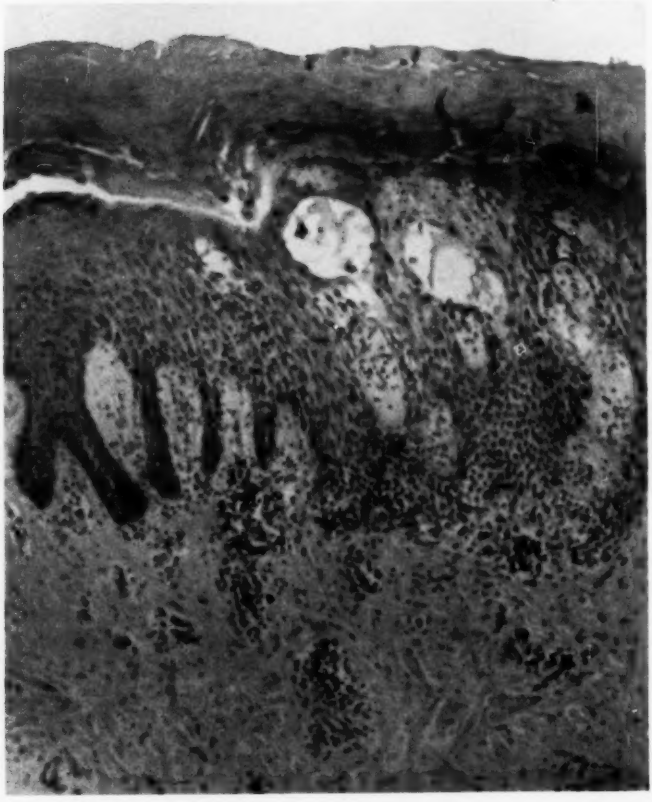

Fig. 8.—Histopathologic specimen of an area seen in Figure 7. Note the parakeratosis and absent granular layer over areas of spongiosis and intraepidermal vesiculation. Hematoxylin and eosin; reduced from mag. × 375.

Fig. 9.—Dyschidrotic dermatitis of the hands two years after a unilateral right dorsal sympathectomy. The left hand has clinical eczematous vesiculation and scaling. The right hand seems only to be desquamating.

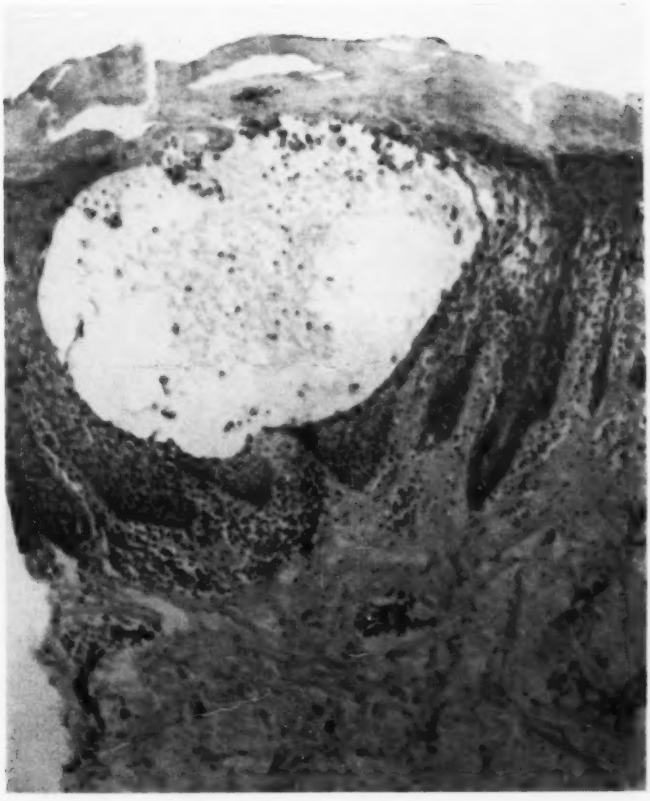

Fig. 10.—Histopathologic specimen taken from the hypothenar area of the left hand (nonsympathectomized). Note the intraepidermal vesicle lying near an intact eccrine sweat duct. Hematoxylin and eosin; reduced from mag. ×390.

years was studied. We explained to him our interest in studying the effect a permanent unilateral dorsal sympathectomy would have on his disease. He agreed to undergo the study. Figure 7 shows a close view of his primary lesions. A biopsy of this area before surgery showed the spongiosis and epidermal vesiculation typical of his disease (Fig. 8).

At all times he has preferred his dry, sympathectomized right hand over his nonsympathectomized hand. Two years after his first unilateral dorsal sympathectomy, at his request, both his lower extremities were made anhidrotic by a bilateral lumbar sympathectomy. Six months later his feet were clinically well, but, by adequate magnification, we could always find minute vesiculation of the "id" type.

Repeated physiological and pharmacological studies proved the sympathectomies to be complete and permanent. Over the years the nonsympathectomized left hand has always shown clinical evidence of the eczema to a greater or less degree. The dry, sympathectomized right hand has always had more scaling and cracking than one would expect from anhidrosis alone. Figure 9 shows them two years after the sympathectomy. At this stage we again studied him in minute detail. Although he liked his dry hand and wanted the other one just like it, we would not agree, not only because of our need for such a control but also because we were not convinced that we had altered his ability to produce spongiosis by such a sympathectomy. The next two biopsy specimens were taken from these hands. Figure

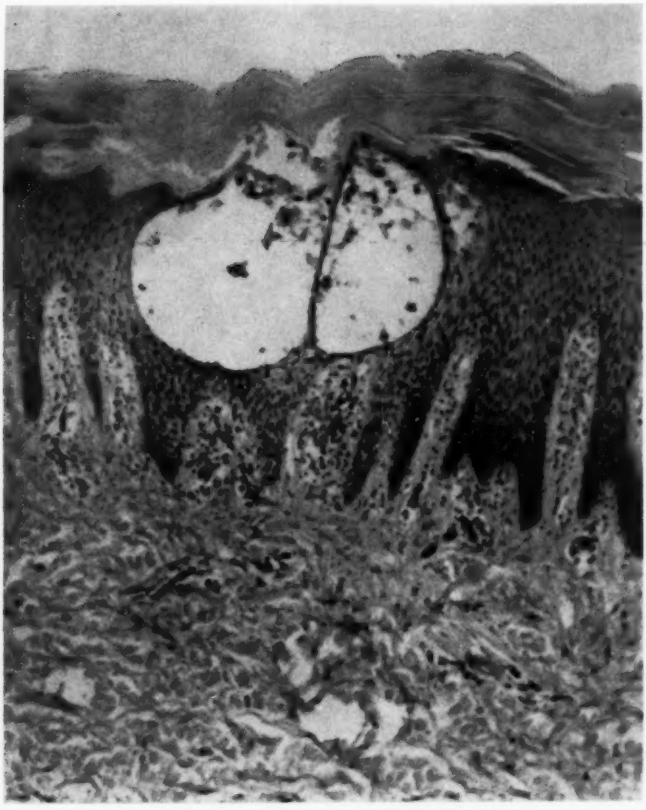

Fig. 11.—Histopathologic specimen taken from the hypothenar area of the right hand two years after a unilateral right dorsal sympathectomy. The sympathectomy had no effect in preventing intraepidermal vesiculation and spongiosis Hematoxylin and eosin; reduced from mag. × 375.

Fig. 12.—The hands of the same patient with dyshidrotic dermatitis 10 years after a unilateral right dorsal sympathectomy.

Fig. 13.—The feet of the same patient with dyshidrotic dermatitis 10 years after a bilateral sympathectomy.

10 shows a biopsy specimen of the eczematous, nonsympathectomized left palm. (Note the uninvolved sweat duct and that it is immune to the spongiosis on either side of it.) Figure 11 shows a biopsy specimen of the dry, scaling sympathectomized right palm, presenting the identical picture. In truth, we had not altered his basic disease of spongiosis and epidermal vesiculation. As additional evidence of this, 10 years after his first operation all four extremities developed vesicular eczematous dermatitis. All three sympathectomies were still complete and permanent (Figs. 12 and 13).

We then focused our attention on atopic dermatitis. This group certainly can produce emotional dermatoses. A cartoon (Fig. 14) taken from the textbook of Pillsbury, Shelley, and Kligman[5] indicates very well the various components that we all diagnose and treat in this disease. The patient with atopic dermatitis is, of course, the real eczema problem. If we use the definition of "atopy" which includes the asthma, hay fever, and eczema groupings, then most of our patients with noncontact eczema are "atopic," in addition to the patient with the classical, disseminated neurodermatitis.

The most intriguing and, of course, the most confusing thing about the atopic is that he has the ability to produce both urticaria and eczema, not only clinically but by skin test. We also know that some antigens have the ability to produce both types of skin tests, immediate-wheal and delayed, and even both types of disease, urticaria and eczema. Penicillin is the classic example. This antibiotic can produce just about all types of allergic disease, including immediate anaphylaxis, serum sickness, urticaria, and contact dermatitis, as well as eczematous "ids."

We have all observed in atopic patients, as well as having read numerous reports about it in the literature, that immediate-wheal antigens can flare a patient's eczema. Perhaps it is because of this that we do not trust the allergic approach or are afraid of it. Yet if we are convinced that our own patients can be made worse by such a procedure, may it not be playing a role in the etiology of his disease if we could only understand it? Once again I found that there are basic rules established in allergy that may be of help.

We know the time element in the skin-test response to sensitization.[6] The 15-minute reaction is a wheal; the 24- to 48-hour reaction is a delayed papule; and the one-week reaction is an eczematous plaque. However, the time element in the process of the natural development of the sensitiza-

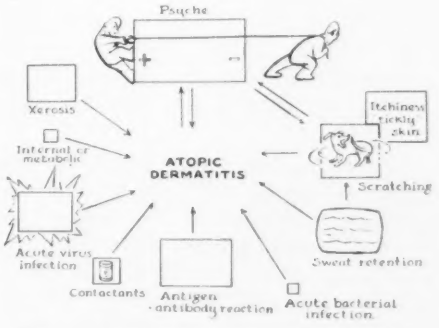


Fig. 14.—Atopic dermatitis. (From Pillsbury, Shelley, and Kligman[6]; reproduced by permission of Dr. Pillsbury and the W. B. Saunders Company.)

tion is just the reverse.[6] The first type of skin reaction to an antigen is an eczematous one. As the host is more chronically exposed to the antigen, the reaction gradually changes to a wheal. The classic example of this is the skin-test reactions of the patient infested with Trichina. Early in the course of the trichinosis the skin test will be positive as a delayed papule at 48 hours. Later in the course of the disease, the skin test will be positive as a wheal in 15 minutes.

As dermatologists, we are more familiar with Trichophyton antigen. In this instance the first skin-test reaction will be an eczematous plaque appearing about five days after the injection. If this is repeated and if the host is exposed to more antigen, the skin-test reaction will be positive as a delayed papule at 48 hours. But in the long, chronic exposure to Trichophyton antigen, as in patients with hyperkeratotic chronic disease of Trichophyton rubrum infections, the skin-test reaction will be an immediate wheal. There are also the patients with T. rubrum infection who show both the 15-minute and 48-hour reactions and possess both hyperkeratosis and vesicular lesions of the palms and soles. Is this type of patient or this type of antigen the exception to the rule, a new rule, or a clue to the bridge between urticaria and eczema?

By now it should be obvious that I spoke the truth when I said earlier that I would raise many questions and not answer them. However, I shall tell you of two more patients before I finish. These patients we look back on as presenting key turning points in our swinging pendulum of thought on this subject.

The first patient was a 48-year-old man whom we saw in 1951 with a history of eczematous dermatitis of the hands of six months' duration, a vague history of "itchy eyes" and "stuffy nose" for many years, and a long history of recurring vesicular eruptions of the fingers that were diagnosed clinically, though not proved, elsewhere as a dermatophytid. Clinically we diagnosed the most recent (six months') episode as an exudative neurodermatitis, not only because it fulfilled Becker's criteria for this disease but also because we were able to rule out contact etiology, Trichophyton sensitivity, etc.

By now we had established a routine of study on these patients whereby we were making ourselves investigate the allergic components of those we were convinced had a form of neurodermatitis and at the same time we were making ourselves investigate the physical, physiological, and personality components of those patients we were convinced had noncontact allergic eczematous dermatitis.

This man received intradermal skin tests to various inhalant allergens suspected from his history. His tests were negative to all of the antigens except those of house dust. At 15 minutes this test showed a positive wheal reaction and at the same time the patient developed itching of his eyelids and a "stuffy nose," which persisted for about four hours. The wheal reaction then faded. Forty-eight hours after the intradermal skin tests, a papular reaction developed in the same area as the skin test with house dust. Simultaneously the patient developed an acute shower of vesicles on his hands and feet of the "id" type. In addition, he developed his first flexural dermatitis in one of the antecubital areas. This clinical and skin-test reaction began to subside in 36 hours. Five days after the intradermal skin tests, the same test area (house dust) again became positive as an eczematous plaque (Fig. 15). At the same time, his exudative neurodermatitis became worse.

Here, then, was a patient who developed all three types of skin-test reactions to one single dose of house-dust antigen, and when the skin-test reactions were positive the various components of his complaints were reproduced. These observations were easy to make, since the patient was in the hospital. But how many patients who receive skin tests from allergists are so observed for delayed reactions to intradermal

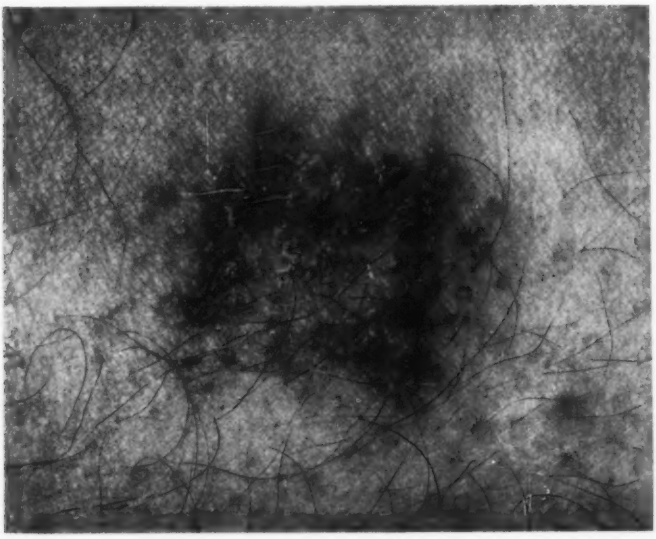

Fig. 15.—In the test site an eczematous lesion developed five days after the intradermal injection of the house dust antigen.

or scratch skin tests and the correlations of such reactions with the general clinical remissions and exacerbations of the specific disease? I am very impatient with allergists who are supposed to know these things who will test a patient with eczematous disease for immediate-wheal reactions only. Previous to this time we were haphazard about such clinical observations, but after this episode we established another rigid routine in our daily practice. We now demand adequate observation of all of our in- and outpatients after they have been skin tested.

Before I present the last patient, let me recall two articles which were published in our own A. M. A. ARCHIVES OF DERMATOLOGY in June, 1957. Drs. Strauss and Kligman [7] show that the internasal, subcutaneous, and surface application of specific protein allergens can cause a flare of an already existing area of contact dermatitis of a different etiology. They interpret their observations as follows: "It is suggested that protein antigens as found in foods, pollens, molds, etc., are not primarily capable of exciting the eczematous or dermatitic reactions, but rather are secondary agents which can produce exacerbations in previously damaged skin sites, whatever their origin." Although we do not necessarily agree with all the interpretations of their observations, the observations themselves are important. In the second article, Drs. Derbes and Caro report [8] a commonly observed, but only occasionally reported, instance wherein, "In an asthmatic patient, not the victim of atopic eczema, patches of eczema appeared at the site of injection after several months of intensive dust vaccine therapy." Once again, here is a correlation in an atopic person, an asthmatic, of an immediate-wheal antigen associated with the production of eczematous lesions.

In 1956 we met a 27-year-old man referred from Arizona (who had not improved there) with severe, nonseasonal, dissiminated neurodermatitis of seven years' duration. He was hospitalized under our care for seven months. He presented every classical, physical, physiological, emotional, psychiatric, and skin-test pattern reaction that has been ascribed to the patient with atopic dermatitis. Several things became obvious as time went on. Every time his skin developed a generalized spontaneous flare, it would have a follicular eczematous component (Fig. 16). The histopathology

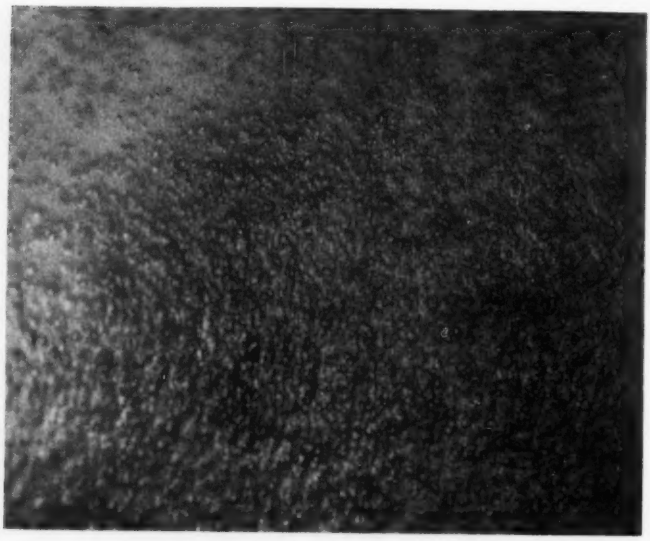

Fig. 16.—The follicular eczematous dermatitis that occurred repeatedly as a spontaneous flare in the patient with disseminated neurodermatitis.

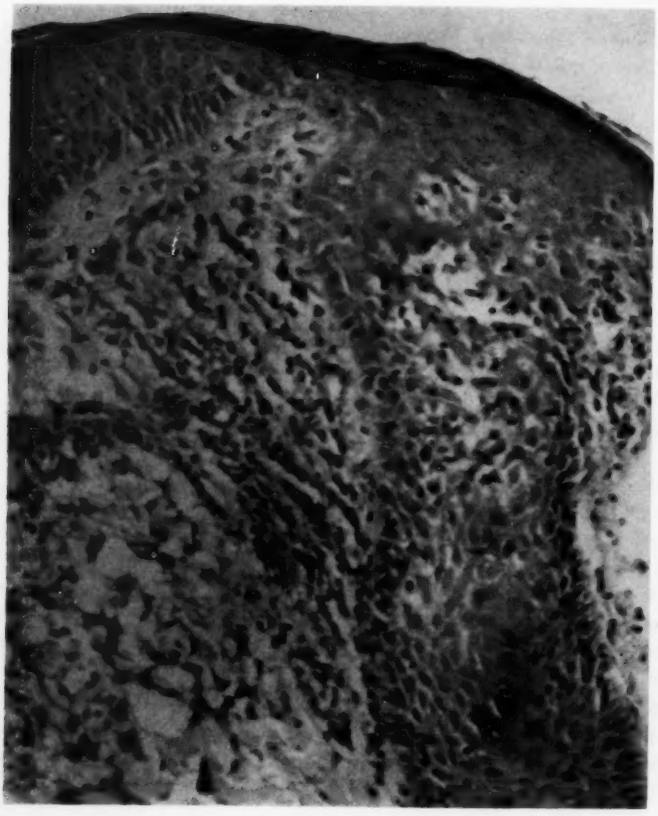

Fig. 17.—The histopathologic structure of a follicular lesion seen in Figure 16 shows primary spongiosis in the hair follicle. Hematoxylin and eosin; reduced from mag. ×630.

*Atopic Dermatitis*

| | |
|---|---|
| 9/13/56: | 10 i. d. Buffered isotonic saline injections<br>No reaction |
| 9/14/56: | Staph. ambotoxoid (1:20) i. d.<br>15 min. 2+ wheal (no systemic reactions)<br>Neg. 24 & 48 hr. reaction |
| 9/17/56: | Mold antigen i. d.<br>15 min. 4+ wheal<br>4-12 hr.: severe asthma (1st attack)<br>Neg. test site at 12, 24, & 48 hr. |
| 9/19/56: | All 10 saline sites positive<br>1 cm.+ eczematous plaques |

of such an area (Fig. 17) showed primary spongiosis in the hair follicle.

When this patient's skin was clear enough for testing, an immediate-wheal reaction was produced by the intradermal injection of molds and Staphylococcus ambotoxoid, but no delayed skin test reactions developed. We then waited until his trunk was entirely free of disease, and on Sept. 13, 1956, introduced into the skin of his back 10 intradermal buffered isotonic saline injections of 0.1 cc. each. No reactions occurred locally or systemically. The following day, Sept. 14, 1956, at a distant site, we retested him intradermally with Staphylococcus ambotoxoid. This was an antigen which had produced an immediate-wheal reaction. He developed the wheal but no delayed skin test or any systemic reaction. Three days later, on Sept. 17, 1956, we introduced at another distant site the mold antigen. A severe immediate-wheal reaction occurred at the site of the injection. Four hours later and of twelve hours' duration, he had his first attack of severe bronchial asthma. The test site was negative at 12, 24, and 48 hours. However, on Sept. 19, 1956, two days after the mold test and six days after the buffered saline tests, all of the buffered saline test sites became positive, infiltrated, eczematous plaques, which on biopsy presented the same histologic picture as his spontaneous flares, i. e., spongiosis in the external root sheath of the hair follicle (Fig. 18).

This is another example of an immediate-wheal protein antigen seeming to act specifically to produce the specific type and localization of spongiosis in a given atopic person once the stage had been previously set, that is, once the skin had been somehow altered to be able to react to the challenge.

We may be thoroughly confused by now, but in reality none of this is new. All of us can recollect similar problems in our

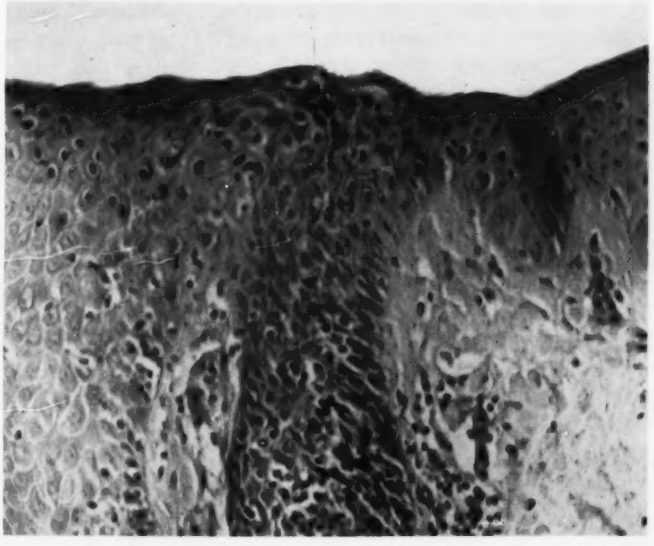

Fig. 18.—The histopathologic structure of the eczematous plaques which developed in the site of a buffered isotonic saline intradermal skin test shows follicular spongiosis. Hematoxylin and eosin; reduced from mag. × 585.

practice as well as in the literature. The evidence is certainly accumulating that the role of an antigen-antibody mechanism seems to be present somehow in these chronic eczema problems. But how? How is the stage set? What are the sequences?

We are not the first persons to be confused by such questions in allergy. If one goes back to the original reports at the turn of the century and over the next 20 to 30 years, when the pioneers in the field were working out the fundamental laws of immunology and allergy as we understand them today, one finds that they, too, were having trouble. They were observing disease in humans and in experimental animals, trying to understand it, and trying to reproduce it. In many instances it was a trial-and-error study of producing antibodies, of stage-setting the host or tissue, and of challenging with specific and nonspecific antigens that finally worked out the sequences and reproducible observations of such things as anaphylaxis, serum sickness, Arthus phenomenon, contact dermatitis, urticarial allergy, etc.

We have much to learn. We are fortunate that some immunochemists and cytochemists are working on the basic problems of the type of immunity that we call allergy. But man is the one who develops atopy and atopic dermatitis, and man, with these diseases, is taken care of by clinicians. As clinicians we can add much to the final understanding of this complex problem if we include in our day-by-day studies on patients a total approach to the diagnosis and treatment of such disease.

Let me say again that in general we in dermatology are a bit prejudiced against the role of allergy in such chronic problems as I have discussed. I was astounded to learn that one of the largest teaching services of dermatology in this country (over 16,000 outpatient visits a year and approximately 50 inpatient beds assigned to dermatology) denies the possession of the antigens of the intradermal or scratch-test variety. I was also surprised last year to hear one of our leading professors in dermatology in this country, a man of highest integrity and sincerity, truly dedicated to the good of dermatology, say, "I don't believe in allergy, but I teach it."

As you know, in the short time I have been on the American Board of Dermatology, I have participated in examining candidates in the field of allergy. I was surprised to find that the majority of candidates taking their American Board Examinations do not know the fundamental ABC's and rules of immediate-wheal and delayed allergies, and, even if they had memorized them for the examination, they could not apply them to the practical problems of the patient.

I proposed this problem to some of the candidates: You have a patient who is an atopic person with a known and proven urticarial allergy to cow's milk. The patient delivers a healthy baby, but three days later a breast abscess develops and she can no longer feed the baby. The pediatrician, knowing of the urticarial problem in the mother, calls you on the phone and asks whether he can safely feed the baby cow's milk or will the baby get hives if he does so.

Most of the candidates obviously guessed "yes" or "no" without reason. One chap belligerently bypassed the question by stating that, from his experience, he did not believe that patients ever got hives from food. But another chap hesitantly said that he thought it would be all right to feed the baby cow's milk but he was not sure. When I asked him why he could say this, he was again hesitant but obviously trying and thinking. I then asked him what my question was really about. He stopped, thought a moment, then brightened up and burst out,

"About atopic reagins."

"Correct! Now answer my original question."

His reaction was as though I had pushed a button on a sorting machine, because in a mechanical voice he said,

"An atopic reagin produces an immediate-wheal reaction, is located in the pa-

tient's serum, can be passively transferred with the serum, is heat-labile, cannot pass the placental barrier. . . . Oh, cannot pass the placental barrier! Yes, yes, it will be all right to feed cow's milk to this baby."

Such questions can be fun and of course a candidate does not rise or fall on such as these. However, it is very discouraging when many candidates cannot even apply the incubation period of contact allergic dermatitis to medicolegal problems in industrial or cosmetic dermatology, problems with which they will be frequently confronted once in practice. In addition, too many candidates could not advise their patients who had been using a tar ointment on their skin to avoid sunlight behind window glass because they did not know the wavelengths that are involved in the various light-sensitivity reactions. It seems that, even though we know these things and we teach these things, perhaps our lack of enthusiasm for allergy does not allow them to be practically implanted in the student's mind.

I know that many in our specialty severely criticize the use of intradermal skin tests in the study of chronic urticarial, eczematous, and atopic skin disease on the basis that they are usually of no help to the doctor and his patient. I want to point out vigorously that there is no branch in medical science that uses an all-or-none attitude toward its diagnostic procedures. We would be the first to condemn the cardiologist if he did not routinely make use of electrocardiography, roentgenography of chest and gastrointestinal tract, peripheral blood cell counts, etc., in addition to his history and physical examination, even if they were apt to be negative, or, if positive, perhaps vague in significance or help to a particular patient.

We all know that the establishment of diagnostic routines and procedures helps a patient in many ways. They establish baseline information about a particular patient to be drawn upon later, if not immediately. They help accumulate information that can be of value over the years in understanding a disease process in general, even if not specifically for any given patient. They form the very foundation for clinical research in every doctor's office and records. They can help the specific patient, also.

We come easy by our morphological diagnoses. We can establish them either by inspection, by palpation, or with an easily obtained biopsy specimen. Perhaps it is too easy and we get both lazy and impatient and thus do not follow a well-established routine to determine the etiology of eczematous and urticarial disease. In our daily practice of dermatology in Hanover, we have included thinking in terms of dermatoallergy and the use of intradermal skin tests in our routines. I have tried to point out to you a few of the reasons why over a 10-year period we have arrived at the use of such disciplines.

Hence, in conclusion, I speak not as one who knows but rather as one who is trying to learn and practice and teach better dermatology. A passive and even a negativistic approach of our specialty toward dermatoallergy is not helping our patients, our specialty, or our profession in the long run.

Before I finish, I must ask myself one more question. Why have I said all this here? I am not certain why. I like to think it is because, having received the honor of presenting the William Allen Pusey Memorial Lecture, this Midwesterner has "come home." "At home" one feels comfortable enough and secure enough to think out loud and to have the purpose of such thoughts truly understood.

Hitchcock Clinic.

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# Dermatitis from Metal Spectacles

*Demonstration of Nickel and Copper Compounds from Corrosion of Earpieces*

**L. EDWARD GAUL, M.D., Evansville, Ind.**

The present undertaking was started when a patient asked about an irritation under the nose pads of her glasses. Upon looking at the frames, a greenish stain was seen under the plastic tubing covering the earpieces. The fact that the temples were gold added to the interest. It was known from the action of jewelry metal on normal skin and in the presence of salt that pure gold was inert, and, furthermore, an alloy of gold and copper was not reactive.[1] The green color may have been due to copper, but nickel also develops greenish compounds. If the color was due to nickel, this fact could prove valuable, as pure nickel and nickel silver (nickel and copper) were not reactive on normal skin or in the presence of salt. Like gold, nickel seemed to inhibit the activity of copper.

A number of opticians were visited, and a collection was made of some of their worn-out, discarded metal frames. Gold-filled and and white gold frames were worn the most. Inspection disclosed that the temples, especially the flexible ends (earpieces), showed all degrees of corrosion. A hand lens was useful in detecting the full extent. Gold and white gold were similarly corroded. Attempts to dismember the earpieces were often thwarted by the destructive action of the corrosive process. Where it was possible to unwind the wire sheaths, spotty excrescences of greenish material were seen.

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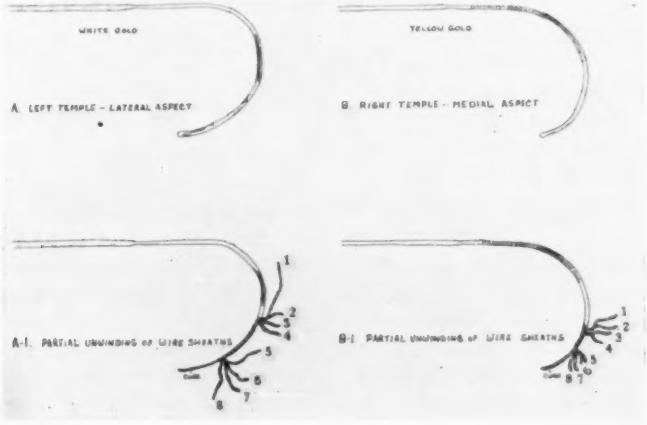
Corrosion of temples of metal spectacles. The flexible end, or earpiece, shows the greatest degree. The sides and inner curvature are the principal sites. *A*. Distribution of corrosion due to contact with the medial surface of the ear. *B*. Corrosion due to contact with the lateral portion of the scalp. The extent is much greater because of more apposition with the skin. *A*-1 and *B*-1 show that as the wires of the outer sheath were unwound, Numbers 1 to 4, more extensive corrosion was encountered; as the wires of the middle sheath, Numbers 5 to 8, were unwound, still more corrosion was found. The core was practically obliterated by the greenish deposit. The wires making up the outer and middle sheaths broke off as they were unwound, because of the destructive action of corrosion on the metal. In new temples, the two sheaths were easily unwound without any breakage. White gold and yellow gold frames were corroded about equally.


WHITE GOLD
A. LEFT TEMPLE - LATERAL ASPECT
YELLOW GOLD
B. RIGHT TEMPLE - MEDIAL ASPECT
A-1. PARTIAL UNWINDING OF WIRE SHEATHS
B-1. PARTIAL UNWINDING OF WIRE SHEATHS

The wires were matted together with the core nearly obliterated by the greenish deposit (Figure).

The distribution of the corrosion corresponded to the site of most intimate contact with the skin. A blotch was seen to outline apposition with the temporal area. The earpieces showed patterns of discoloration where they touched the scalp and ears. Corrosion affected the nose pieces and the area where the butt of the temples was attached to the eyepiece. The latter would be discolored if the metal had rested upon the infraorbital skin. The opticians stated that corrosion was not limited to any one make of metal spectacle frames.

### Purpose of Investigation

If the greenish deposit was due to a nickel compound, it was felt that it might be possible to reproduce on the skin the formation of a nickel compound. The demonstration of the components needed for the reaction might in turn help to explain the origin and development of nickel sensitivity.

*Construction of Earpieces.*—A new set of gold-filled temples was obtained for dissection. Examination with a hand lens revealed that flexibility was achieved by means of wire sheathing. The free end of the earpiece was snipped off, and, with the aid of a probe, it was possible to unwind the outer layer. This earpiece was constructed from four separate wires, each of which measured about 1 mm. wide and 0.5 mm. thick. The outer sheath was removed to the point where it was soldered to the butt of the temple. Now another layer was seen. It had the same construction as the outer, and it was unwound in the same manner. The central portion consisted of a core of twisted wire about 0.5 mm. in diameter.

The materials for testing were taken from the earpiece. A wire from the outer sheath was cut into pieces about 1 cm. long. Similar cuttings were taken from the middle sheath and core. An intact earpiece was also cut into test samples. Jagged ends were covered with a narrow strand of adhesive to prevent injury to the skin. The identification mark on the temple from which the earpiece was taken was sent to the manufacturers, who furnished the approximate composition.

### Action of Earpiece Samples on Normal Skin and Adhesive

Volunteers were used for patch tests. They were the same as employed earlier except for the male patient, aged 48.[1] The test samples numbered four, and the patch tests were done on the forearm with use of conventional elastic adhesive (Elastoplast)

TABLE 1.—*Action of Earpiece Samples on Normal Skin and Adhesive*

| Composition | Outer Sheath | Middle Sheath | Core | Intact Earpiece |
|---|---|---|---|---|
| | Wire core Ni, wire shell, 12K gold | Cu 68%<br>Ni 15%<br>Zn 17% | Cu 90%<br>Sn 9.8%<br>P 0.2% | |
| Luster and color | Shiny gold | Shiny silver | Dull bronze | Shiny gold |
| Tape | | | | |
| Coral | | | | |
| Green deposit | | | | |
| Corrosion | | | | |
| Green deposit | | 1 | 1 | 3 |
| Skin changes | | | | |
| Symptoms | | | | |
| Green deposit | | 1 | 1 | 3 |
| Patch tests | | | | |
| Erythema | | 2 | 4 | 3 |
| Vesicles | | | | |
| Duration | | | | |
| 3 days | | | | |
| 5 days | | | | |

TABLE 2.—*Action of Earpiece Samples with Salt on the Skin*

| Composition | Outer Sheath | Middle Sheath | Core | Intact Earpiece |
|---|---|---|---|---|
| | | Cu 68% | Cu 90% | |
| | Wire core Ni, | Ni 15% | Sn 9.8% | |
| | wire shell, 12K gold | Zn 17% | P 0.2% | |
| Luster and color | Shiny gold | Shiny silver | Dull bronze | Shiny gold |
| Tape | | | | |
| Coral | | 4 | 6 | 3 |
| Green deposit | 1 | 4 | 2 | 5 |
| Corrosion | | | | |
| Green deposit | | 6 | 4 | 5 |
| Skin changes | | | | |
| Symptoms | | 2 | 3 | 6 |
| Green deposit | 2 | 4 | 3 | 6 |
| Patch tests | | | | |
| Erythema | 2 | 3 | 6 | 6 |
| Vesicles | | 1 | 1 | 2 |
| Duration | | | | |
| < 3 days | | 3 | 4 | 6 |
| > 5 days | | 1 | 2 | 2 |

patches. The tests were read in 24 hours, and the results are shown in Table 1.

The earpiece was by far the most reactive. The cut ends showed the greatest degree of corrosion. Three subjects showed a greenish deposit on the skin. The hand lens was necessary for detection of the green deposit in two subjects. The middle sheath wire in one subject showed a greenish deposit, and the core itself showed a similar deposit in another subject. The outer sheath appeared to be inert on normal skin. The only reaction from the test samples on normal skin was a mild erythema, which disappeared in a day or so. The absence of any coral staining on the tape aroused suspicion that copper was not responsible for the greenish deposit.

### Action of Earpiece Samples with Salt on the Skin

These patch tests were done as those on normal skin; the same subjects were used, but to each metal sample about 3 mg. of salt was added before covering with the patch. The results are recorded in Table 2. Coral staining on the tape developed from the middle sheath in four subjects, the core in six subjects, and the intact earpieces in three subjects. It was faint and inconspicuous compared to that from copper. A greenish deposit was seen on the tape from all the samples, but notably from the earpiece and middle sheath. The greatest degree of corrosion affected the middle sheath, earpiece, and core. It was seen to extrude from the cut ends of the earpiece like froth formation. The hand lens disclosed a packing of it between the margins of the wires making up the outer sheath. In some places, it extruded sufficiently to form little nodes. These findings helped to explain the distribution of the corrosion found in worn-out earpieces. Seemingly, the core and middle sheath were the most easily corroded. The occurrence of symptoms from the patch tests was looked upon with great interest. They coincided with the complaints from patients about their glasses. Burning was the most prominent symptom, and this was sufficient to cause removal of the patches in less than 12 hours in two subjects. The earpiece produced symptoms in six subjects. The presence on the skin of a heavy greenish deposit was associated with the development of symptoms.

The greatest difference when patch tests with the metal samples on normal skin were compared with those in the presence of salt was the severity of reactions. There were present a bright erythema and flaring edema and, at the point of contact with the metal,

a mass of vesicles. The erythema in one subject persisted almost six weeks. Two subjects developed vesicles, and their reactions persisted over five days. The intensity of the patch-test reactions was evidence that the greenish deposit was far more irritating than the greenish compound from copper.[1]

### Chemical Analysis of Greenish Deposit on Earpieces

The desire to know the nature of the greenish deposit was made known to Walter Wolman of the Chemical Laboratory of the American Medical Association. Following is his report from Dr. Gordon Schrotenboer in the Chemical Laboratory: "The tests showed that both nickel and copper salts were present, but the degrees of positiveness of the tests showed that the major portion of the green deposit was a nickel compound."

### Summary

The nature of the greenish deposit formed by corrosion of metal spectacles has been found to be a compound of nickel, probably admixed to some extent with a compound of copper. Patch tests showed that these corrosion products were primary irritants. The irritants may be the avenue by which eventual sensitization to nickel develops. The reaction to the middle sheath wire was looked upon with much interest because an alloy of copper and nickel proved to be nonreactive, while an alloy of copper, nickel, and zinc was reactive. The action of zinc in the alloy is under suspicion. The core of the earpiece was also reactive, and so apparently tin and phosphorus do not prevent the reactivity of copper.

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# Nevus Lipomatosus Cutaneus Superficialis (Hoffmann-Zurhelle)

*Presentation of a Case and Review of the Literature*

FRANCIS W. LYNCH, M.D., and ROBERT W. GOLTZ, M.D., Minneapolis

The following case report is presented because of the comparative rarity of this nevus. To our knowledge, only eight reports of this condition have appeared in the world's literature, only two in America.

Nevus lipomatodes cutaneus superficialis was the title given by Hoffmann and Zurhelle [1] to a nevoid anomaly consisting of grouped papules and nodules which on histologic examination showed the presence of ectopic fatty tissue in the corium. The second case was described by Robinson and Ellis in 1937.[2] In more recent years cases have been presented by Nikolowski,[3] Kúta,[4] Thöne,[5] Holtz,[6,7] Blumenthal,[8] and Hering.[9]

Enough similarity exists in the clinical and histologic findings in all reported cases that there can be little doubt that this is an entity. Usually, at least part of the nevus had been present at birth, though there has often been extension of the lesion during childhood. In Holtz's patient, however, the nevus appeared at 18 years of age. Notable is the predilection of this nevus for the region of the pelvic girdle. The reported sites include the buttocks, sacral and coccygeal region, and various surfaces of the upper thighs. The greatest deviation was in the case of Kúta, where the lesion was on the right side near the angle of the ribs.

Typically, plaques measuring up to 8×15 cm.[6,7] are made up of groups of nontender papules and nodules, often arranged in linear or systematized distribution, sometimes following the lines of body folds. The papules have been as small as pinhead size, elevated only a millimeter, up to confluent nodules 2×0.5 cm., elevated 1 cm. above the surrounding skin surface. The color is the same as nearby normal skin or pale yellow or yellow-red. The surface is usually smooth but may be irregularly folded or even warty. The consistency is invariably soft, and some of the nodules can be pressed down into the skin in a manner reminiscent of macular atrophy.

Histopathologically important is the presence of fat cells in the middle and deeper portions of the corium. The strands of fat cells are of variable size and may in the aggregate occupy a large part of the corium, being separated only by remnants of collagen in the form of septums. They do not extend into the papillary portion of the corium and may or may not be continuous with the subcutaneous fat. There is often a grouping of these fat lobules around appendages and, particularly, blood vessels.

Epidermal changes, while usually present, appear to be secondary. They consist of hyperkeratosis with follicular plugging, moderate acanthosis with squaring of the rete pegs, and hyperpigmentation of the basal layer, sometimes associated with increased deposition of melanin in the upper part of the corium. The epidermal changes, therefore, resemble those of epidermal nevi.

Considerable discussion has centered around the histogenesis of this nevus. Hoffmann and Zurhelle found the collagen fibers surrounding the masses of fat cells to be degenerated, consisting of fine fibers which stained only weakly with the usual connective tissue stains. The areas of loose con-

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From the Division of Dermatology, University of Minnesota, F. W. Lynch, Director.

nective tissue stained metachromatically with polychrome methylene blue and crystal violet. In this region the elastic fibers were also fragmented. These authors were led to the conclusion that the deposition of fat is secondary to some primary degenerative change of the connective tissue. This opinion was concurred in by Nikolowski, who found similar degenerative changes and metachromasia in the connective tissue in his cases.

On the other hand, Robinson and Ellis expressed the opinion that the fat cells in the cutis represented a nevoid anomaly and were not the result of degeneration of the collagen. Kúta and Thöne also found little evidence of degeneration of collagen and no metachromasia. The elastic fibers, though fine and fragmented, were present. These authors also interpreted the histogenesis to represent heterotopic development of fat in the corium, with only secondary collagen change.

The most thorough study of this question was carried out by Holtz, who demonstrated, in addition to large mature fat cells, less mature forms comparable to those found in embryonic panniculus adiposus. These apparently arose from the wall of the venous capillary around which the abnormality centered and grew into the surrounding connective tissue, which persisted as very fine collagen, elastic, and reticulin fibers reaching from the unaffected connective tissue to the wall of the central vessel. On staining with crystal violet and thionine, metachromatic substance was found to be adherent to the fibrils. Holtz, therefore, concluded that the primary change is a growing out of primitive "preadipose" tissue from blood vessel walls. Edema and invasion of the surrounding connective tissue result in its destruction. The young adipose cells then progressively take on fat and at last come to be identical with mature cells of the subcutaneous layer. This process corresponds to that described by Wassermann [10] in the embryonic development of normal fatty tissue and in lipomas.

## Report of a Case

A woman,* 18 years of age, first noted plaquelike thickening of the skin of the upper portion of the left buttock at the age of 13. This gradually enlarged without symptoms, except possibly very slight itching. There was no treatment. The patient's general health was good, and there was no evidence of other nevoid disorders.

On the upper portion of the left buttock was a group of pale yellow, slightly elevated and thickened rounded papules 2 to 4 mm. in diameter in an area about 5 cm. in diameter. (Fig. 1)

*Histopathologic Findings.*—The epidermis shows marked hyperkeratosis of a basketweave variety, and the follicular orifices are dilated and plugged by loose keratin (Fig. 2). The rete is either thinned or acanthotic, with some sharpening of the corners of the rete pegs. The basal layer contains moderate amounts of melanin. The over-all epidermal structure is, therefore, reminiscent of epidermal nevi.

* This patient was presented before the Minnesota Dermatological Society on Feb. 22, 1958.

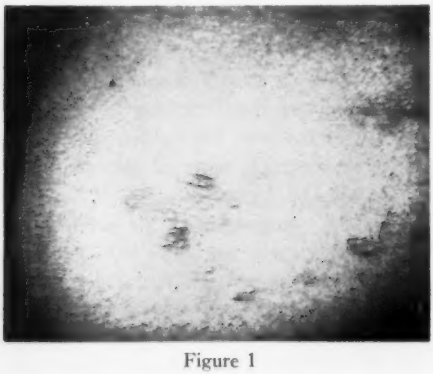

Figure 1

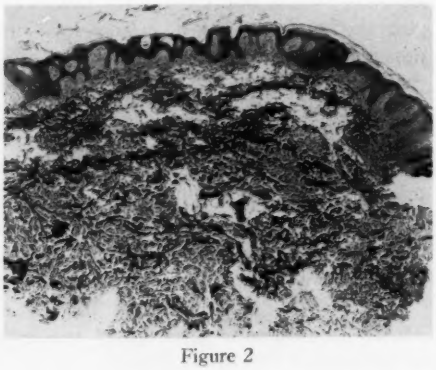

Figure 2

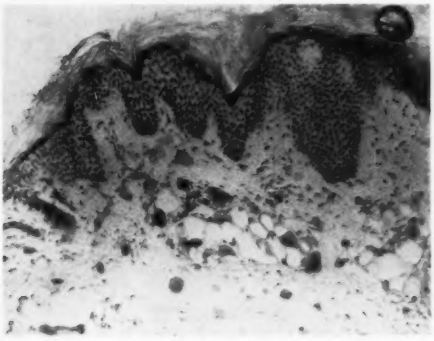

Figure 3

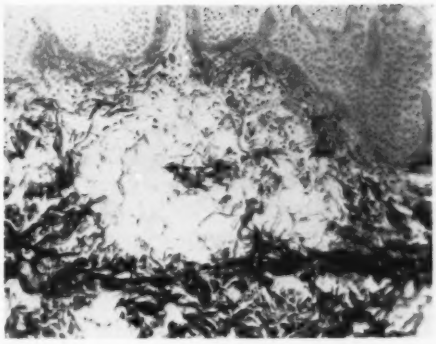

Figure 4

The papillary corium is essentially normal. Immediately beneath it, extending transversely, is an extensive deposit of fatty tissue which almost completely separates the papillary portion from the deeper parts of the corium. This band is penetrated here and there by strands of collagen. Numerous dilated blood vessels can be seen coursing through the area of fatty tissue, and in some places the fat cells follow the vessels as they ascend toward the papilli, while in the deeper part of the corium fatty tissue surrounds the larger blood vessels as they rise from the hypoderm. The fat-containing cells appear mature. Groups of these fat cells are separated by narrow strands of collagenous connective tissue, the fibers of which are of approximately the same diameter as the collagen fibers in the papillary portion of the corium. They stain slightly less intensely with eosin than the thicker collagen fibers elsewhere in the cutis. Sudan III shows the fat cells in the corium to take the same bright orange stain as the cells of the subcutaneous layer (Fig. 3).

With the Van Gieson stain the collagen fibers appear normal except where interrupted by the fat deposits (Fig. 4). Collagen directly adjacent to the fat cells has normal staining properties, as do the fibers running in the septums between the cells. The Weigert elastic tissue stain shows the elastic fibers to be preserved and, in fact, to run between the individual fat-containing cells in some places. There is no evidence of fragmentation or loss of elastic tissue fibers (Fig. 5).

With the periodic acid-Schiff reaction, no abnormality of the connective tissue or ground substance is noted (Fig. 6). The cell membranes of the fat-containing cells are Schiff-positive; the blood vessels which run through the center of the fat globules are prominent because of the positivity of their endothelial lining.

No metachromasia is noted after staining with toluidine blue.

In summary, the findings in our case support the view of Holtz that the primary disturbance in this nevus is the growth of adipose tissue from the walls of blood vessels and that degenerative changes in the connective tissue, if present, are secondary phenomena. No significant degenerative changes in the connective tissue are demonstrable in our sections.

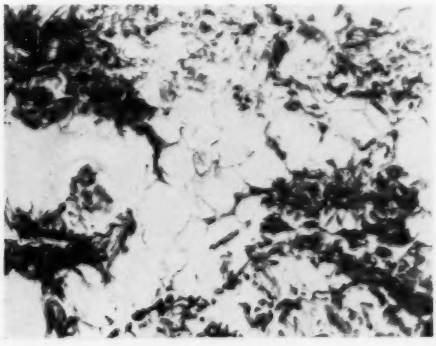

Figure 5

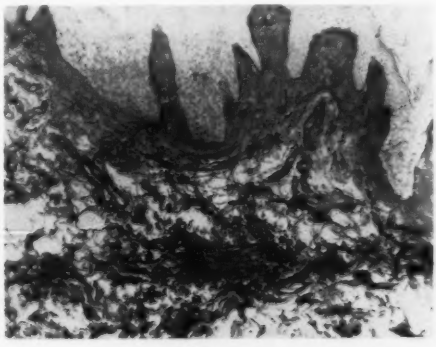

Figure 6

## Comment

This nevus, though undoubtedly rare, has probably escaped recognition in the past. Hoffmann and Zurhelle and Nikolowski have listed previously reported cases which may have belonged to this group. All of these cases were either clinically atypical or not confirmed histologically. This condition is probably most easily confused clinically with other types of connective tissue nevi, sebaceous nevi, or grouped lesions of macular atrophy and histologically with lipoma and perhaps also epidermal nevi. The clinical characteristics of this nevus prevent confusion with lipoma, while standard reference works on dermatologic histopathology are unanimous in stating that lipomas are subcutaneous tumors. Their extension into the skin has not been described to our knowledge.

The predominant localization of these nevi around or near the pelvic girdle has provoked comment by several authors. The reason for it remains unknown. Nikolowski speculated about some peculiarity of the circulation in that region and also pointed out that the gluteal area is subjected to lasting pressure and tension during intrauterine life. Holtz pointed out that this area of the body is "lipophilic," that is, the fat pad is normally thick here, and this is frequently a site of predilection for other disorders of fat, such as lipodystrophies and dystrophia adiposogentalis. On the other hand, as Günther pointed out,[11] lipomas are relatively rare in this region.

## Summary and Conclusions

An instance of nevus lipomatosus cutaneus superficialis (Hoffmann-Zurhelle) occurring in the gluteal skin of an 18-year-old woman is described. This is the third case to be reported in America and the ninth in the world's literature.

The histopathologic findings in this case support the view that the primary disturbance is an ectopic growth of adipose tissue arising from the blood vessels of the corium, not resulting from fatty degeneration of the connective tissue.

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# A Unique Case of Trichorrhexis Nodosa—"Bamboo Hairs"

EARL W. NETHERTON, M.D., Cleveland

In 1949 I examined a little girl who had a congenital ectodermal defect manifested by a unique type of fragilitas crinium which, so far as I have been able to determine, has not been discussed in the literature. I have been diffident about reporting my findings because the patient lived in a distant city and, therefore, was unable to remain under prolonged observation. However, a résumé of her history, together with mounted hairs or photographs of them, has evinced such interest among several eminent dermatologists that I am encouraged to believe that such a rare type of fragilitas crinium warrants this report.

Submitted for publication May 24, 1958.

Emeritus Member of the Staff, Department of Dermatology, The Cleveland Clinic Foundation, and The Frank E. Bunts Educational Institute.

## Report of a Case

A girl, aged 4 years, was admitted to The Cleveland Clinic on Nov. 22, 1949, because the hair on the scalp had failed to grow to normal length (there had been no area of baldness), and a pruritic eruption had been present since birth. The mother stated that at birth the patient's entire cutaneous surface was extremely red and that for several weeks thereafter there was a generalized exfoliative dermatitis emitting a foul odor. The erythroderma gradually disappeared, leaving a persistent papular squamous eruption disseminated over the trunk and the extremities. Partial remission of this eruption occurred during each summer season, although it had never disappeared entirely.

Fig. 1.—Photograph of patient when 11 years old, showing lack of hair on sides and back of scalp. Hair failed to grow to normal length.

Fig. 2.—Photograph of patient's back, showing chronic dermatitis that resembles chapping (age 11 years).

At the age of 2 years, the patient had had vaccinia. Since infancy she had had frequent attacks of upper respiratory infection. The mother stated that the child was "frequently restless, irritable, and difficult to feed because of her preference for liquid foods."

There was no familial history of hay-fever, asthma, or eczema. Two siblings, aged 8 and 2 years, were normal.

Physical examination disclosed that the patient was thin and poorly nourished. The skin was abnormally dry, and there were poorly demarcated areas of pink scaly dermatitis on the forehead and neck. There was excessive seborrheic scaling on the scalp, but there were no follicular keratosis pilaris-like papules on the scalp. Patches of subacute erythematous scaly dermatitis which resembled chapping were scattered over the trunk and extremities, as well as groups of small discrete acuminate pink follicular papules (Fig. 2). Some of these papules had apical keratotic spines. Pruritus was paroxysmal and was said to be usually severer during the night. The teeth and nails were normal. The lymph nodes of the neck, axillae, and inguinal regions were palpable. The spleen and liver were not enlarged.

There were no significant abnormal physical findings other than the eruption and changes involving the eyelashes, eyebrows, and hairs of the scalp. The hair on the scalp was dry and fragile and lacked the luster and beauty commonly seen in the hair of young girls. Hairs on the occiput and sides of the scalp were no longer than 3 or 4 cm. (Fig. 1) and developed transverse fractures so easily that it was difficult to remove them from the follicles by traction. Casual inspection did not reveal nodes involving the hairs of the scalp.

Microscopic examination of hairs from the scalp and the eyebrows revealed a unique type of nodosity or jointed swelling of the hair shafts. Apparently the jointedness accounted for the easy fracturing of the hair shaft and its failure to grow to a normal length. Some eyelashes and downy hairs from the arms showed small nodes, but they were not the well-developed jointed swellings of the type seen in the hairs from the scalp.

A biopsy specimen from the scalp unfortunately was not obtained. However, tissue from an erythematous plaque on the patient's back was removed. Sections from this biopsy specimen revealed surprisingly few significant histopathologic changes. The hair follicles and accessory glands were normal. The epidermis was normal except for small areas of parakeratosis. There was mild edema and inflammatory perivascular infiltrate in the upper corium.

The most fascinating findings were the polymorphic abnormalities of the hairs from the head. The variations ranged from slight rotation along the axis of the hair, with a wave-like irregularity of the cortex of the hair shaft, to well-developed jointed nodes that resembled the joints of a bamboo pole. The nodes varied in size and were irregularly distributed along the hair shaft.

Almost seven years after the initial examination, in September, 1956, I had the privilege of examining the patient again in her home city. The hair on the scalp was dry, without normal luster, and was fragile. The hair on the sides and posterior surfaces of the scalp had failed to grow to normal length. Hairs removed from the scalp showed the same unique type of joint-like nodose swelling of the shaft which was observed at the first examination in 1949. Likewise, additional biopsy specimens of skin taken by her family physician showed changes identical with those observed in 1949. The skin of all areas was abnormally dry, and there were numerous areas of squamous dermatitis which resembled chapping. There were groups of small acuminate skin-colored follicular papules scattered over the trunk and extremities. The skin in the cubital and popliteal fossae was thickened. Pruritus was present but said to be not troublesome. Seborrheic scaling of the scalp was not profuse.

### *Laboratory Studies*

Hairs from the scalp were mounted in balsam, for study of the morphologic details of the hair shafts. The nodose swellings showed great variation in size (Fig. 3). The earliest indication of abnormality comprised a narrow indentation of the cortex of the hair, forming a shallow sulcus, which appeared to surround the shaft. This change was sparse or frequent, occurring at irregular intervals and throughout the length of the hair. One hair showed early indentation of the atrophic portion of the shaft, immediately distal to the orifice of its follicle. As the abnormality had progressed, swellings of the shaft had developed, the sulcus had enlarged, and, on the proximal portion of the hair shaft, a concavity had formed into which fitted the adjacent enlargement of the distal portion of the hair. These combined changes had resulted in the formation of a pseudojointed nodose swelling that, as previously stated, closely resembled the appearance of the joints of a bamboo pole.

Changes observed in the large nodes suggest that there had been an invagination or intussusception of portions of the hair shaft. An additional component of the abnormality of growth of the hair shaft is a granular degeneration that is manifested by the presence of clumps both of fine and of larger black granules in areas of the hair shaft and more particularly within the medullary portion of some hairs. A dense concentration of these granules may be seen in the concave portion of the jointed swellings. Complete fracture of the hair

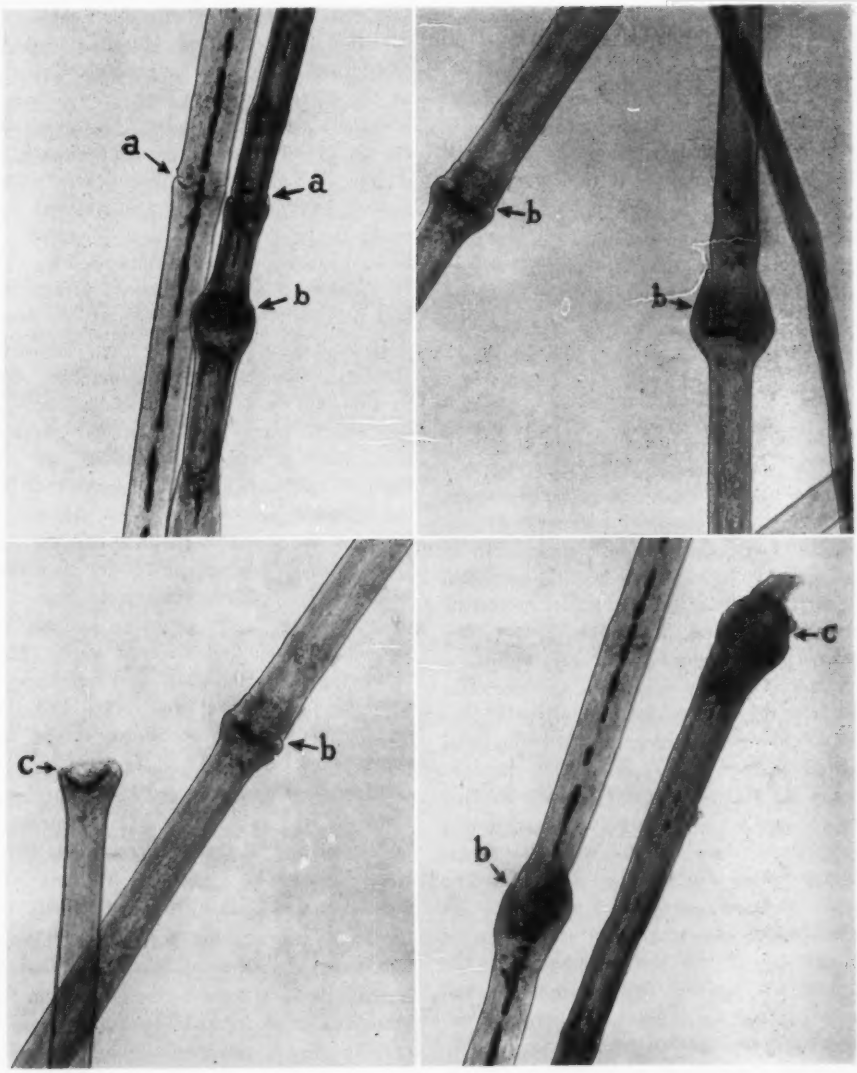


Fig. 3.—Photomicrograph showing nodose swelling of hair shaft which resembles joints of bamboo. (*a*) Early indentation of cortex of hair shaft; (*b*) polymorphic joint-like nodes; (*c*) concavity of hair shaft at the point of fracture.

occurs at the site of the nodosity, and much of the dark granular substance remains within the cupped end of the proximal portion of the hair. It is believed that the granules are not an infectious organism. Cultures of hairs planted on Sabouraud's medium did not show growth of a pathogenic fungus.

*Comment on Case*

The dermatosis that this patient showed is considered to originate from a congenital ectodermal defect. The dry ichthyotic skin and the erythematous scaly dermatitis that persisted from birth are manifestations

compatible with the diagnosis of a dry type of erythroderma ichthyosiforme congenitum. It is significant that there was no change in the characteristics of the eruption or abnormalities of the hair during the seven-year interval between the first and the second examination of this patient.

It is regrettable that a biopsy specimen of the scalp was not obtained. A study of serial sections of the hair papillae might have added much valuable information, as the mechanism of formation of the nodes is obscure.

## Comment

The most familiar diseases in which fragility and nodose swellings of the hair shaft are prominent characteristics are trichorrhexis nodosa and monilethrix. Nodose swellings that resemble those seen in trichorrhexis nodosa have been observed in pili torti.[1] Nodular concretions of infectious origin surrounding the hair shafts in piedra nostros and lepothrix differ greatly in appearance from those seen in trichorrhexis nodosa and monilethrix. Formerly, the concept was widely accepted that abnormal changes involving the hair shaft in trichorrhexis nodosa are of infectious origin. This concept now has been largely discarded, and the present consensus is that the longitudinal splintering of the shaft and the formation of nodes, which resemble the interlocking of two small brushes at sites of fracture of the hair shaft, probably are the sequelae of too-frequent shampooing and excessive dryness of the hair. Some chemicals commonly applied to the hair may be important etiologic factors.

Pili torti and monilethrix are examples of ectodermal defects.[2] Monilethrix usually is hereditary[3] and is characterized by numerous small discrete papules, similar to those of keratosis pilaris, on the scalp, and sparse growth of short fragile beaded hair. The nodose swellings are uniform in size and shape and are located at regular intervals throughout the entire length of the hair. There is notable constriction of the hair shaft between the nodes. Abnormal dentition and other manifestations of the ectodermal defect may be present. Twisting of the hair around its long axis occurs in some of the beaded hairs. However, this change is minor and does not approach the degree of rotation seen in pili torti. Danforth[4] has pointed out that normal hair tends to be ribbon-like and frequently is rotated to some degree around the long axis. He believed that this feature of normal hair had been neglected by previous observers.

It is illogical to surmise that the varied abnormal changes involving the hair shaft in the case just reported could occur in progressive stages in the lifeless shaft of an adult hair. As in monilethrix, the primary disturbance probably occurs within the hair papillae. In this case, the unique features are the abnormalities of the hair shaft, which were responsible for its failure to grow to a normal length. In regard to this case, Drs. M. F. Engman, Lee McCarthy, Herman Pinkus, Richard Weiss, Harold Cole, Fred Weidman, and others, were unanimous in stating that never had they seen similar nodosa swellings of the hair shaft.

After observing mounted hairs, Engman[5] stated: "It does not look like trichorrhexis nodosa or any of the hair conditions that I have ever seen or know of." He also commented that the nodes "looked exactly like the joints in a fishing pole" and suggested the name of "bamboo hairs." McCarthy[6] stated: "I have come to the conclusion that you have in all probability a new type of hair atrophy, a possible variant of trichorrhexis nodosa. . . . Certainly, the photographs show the bamboo-like disturbances of the hair beautifully." He was of the opinion that the nodes resulted from "a disturbance in the hair papillae which later resulted in an abnormality of the adult hair." Pinkus[7] wrote: "The hairs of your case are most remarkable, looking, as you say, like the knots of bamboo or in some instances almost like the joints of equisetum (horsetail) with one end inserted into the cuff-shaped

other half. . . . I do not remember that my father mentioned anything similar. I also consulted his book on diseases of the hair. . . rummaged in the old reprint collection of my father, but could find nothing comparable."

## Summary

A case is reported of unique type of atrophy of the hair with fragility and nodose swellings of the hair shaft, which grossly resemble the joints of bamboo. Hair of the scalp was most particularly involved; however, eyelashes, eyebrows, and hair on the arms were similarly abnormal.

The fragilitas crinium and concomitant eruption are considered to be essential components of a congenital ectodermal defect. The eruption resembled the cutaneous features of the dry type of erythroderma ichthyosiforme congenitum.

The Cleveland Clinic, 2020 E. 93d St., (6).

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# Woolly Hair Nevus

*Report of a Case*

**CHARLES F. POST, M.D., New York**

In April, 1927, Dr. Fred Wise reported on "a peculiar form of birthmark of the hair of the scalp, hitherto undescribed, with report of two cases."[1] With this report Wise originated the term woolly hair nevus. The case reports concerned two 5-year-old girls whose families were unrelated, both of whom showed light woolly hair on one portion of the scalp, while the rest of the hair was straight and brown. One of Wise's original cases showed a linear nevus of the skin of the back of the neck, right elbow, and wrist, ipsilaterally with the woolly hair on the scalp. Wise justifies the use of the term woolly hair nevus by stating that birthmarks of the hair are changes in the "color, consistency, structure, and morphology of the hair shaft."

The next report (Wise and Sulzberger) of a similar patient was of an adult male with kinky black hair growing over the frontal, temporal, and parietal areas of the scalp.[2] This abnormality appeared, apparently, in adult life.

No further cases can be found until the one presented by Anderson at the Los Angeles Dermatological Society in 1943.[3] This was a 5-year-old girl who had a light-brown nevus of the skin on the same side as the woolly hair nevus of the scalp. In 1948 Sweitzer presented a case at the Minnesota Dermatologic Society that does not, in my opinion, qualify as a genuine woolly hair nevus.[4]

More recently, the German literature contains three case reports of this aberration of hair growth. Hoffmann's patient showed considerable seborrhea of the woolly hair portion of the scalp.[5] Knierer's case strongly resembles the adult case reported by Wise and Sulzberger.[2] The case of Born fits Wise's original description very well.[7] There was no family history of a similar abnormality in any of these cases. The case reported herein is the eighth case appearing in the medical literature.

## Report of Case

The patient was a 7-year-old white boy of Polish-Irish extraction. He was seen for an eruption on the back that proved to be impetigo. In the course of routine examination of his skin, it was noted that he had two distinctly different kinds of hair, namely, straight brown hair and blonde curly hair. Additionally, verrucous, brown, linear lesions were noted on the right side of the face, neck, and right arm.

The mother stated that the child was born with fine brown hair on the scalp. When he was 2 months of age, a half-dollar-sized area of curly blonde hair appeared on the right temple. From that time until he was 4 years old, this area of curly hair gradually spread to the right temple, posterior parietal, right postauricular, and right occipital areas of the scalp. The only apparent change during the past three years has been some darkening of the blonde hair, but the curliness has persisted unchanged. At about the time that the first area of curly blonde hair was noted, areas of dark rough skin appeared on the right side of the face, neck, and right arm.

*Past History and Family History.*—Both paternal grandparents were Irish; both maternal grandparents were Polish. The patient's parents were born in the United States. The patient is the third of five children. The parents are not related in any way. The mother has had no miscarriages, and all pregnancies resulted in normal, full-term, spontaneous deliveries. There are no cutaneous abnormalities in the patient's siblings. Both of the parents are in good health; their hair is normal.

Submitted for publication May 14, 1958.

From the Department of Dermatology, Columbia University College of Physicians and Surgeons and the Presbyterian Hospital.

Woolly hair nevus.

The patient's father has two 1.5 cm. nevus flammeus lesions on the right cheek.

The patient has had diphtheria, pertussis, tetanus, and smallpox immunizations. His only childhood illness was chickenpox. There have been no serious illnesses, accidents, or operations. The mother states that the child was given soybean milk feedings from the age of 3 months to 2 years because of mild eczema of the face, presumably caused by milk. Further system review is entirely negative.

*Examination.*—The general appearance is that of a normal, healthy, 7-year-old boy. Exclusive of the cutaneous findings and enlarged tonsils with associated cervical lymphadenopathy, complete physical examination is normal.

There are a few scattered small light-brown pigmented nevi on the face, neck, and trunk.

On the right side of the neck, right preauricular area, right upper trapezius area, and extending down the lateral aspect of the right arm onto the palm of the hand and right thumb there is a dark-brown verrucous nevus.

The scalp hair is of normal distribution. There is no seborrhea or alopecia. Extending from just in front of the right ear, there is an even growth of blonde curly hair that covers the right parietal, parieto-occipital, and occipital areas of the scalp. The linear nevus seen on the neck, shoulder, arm, and hand cannot be detected visibly in the scalp. The rest of the scalp is covered with straight brown hair of normal appearance.

The distribution and growth of hair on the rest of the body are normal. The fingernails and toenails are normal.

Microscopic examination of the blonde curly hairs and straight brown hairs from the scalp shows no evidence of monilethrix, trichonodosis, trichorrhexis nodosa, or other associated abnormalities.

## Summary

Although it may be of academic interest only, three types of woolly hair nevus appear to emerge from the reported case histories: (1) woolly hair nevus without any visible changes of the glabrous skin or scalp itself, (2) woolly hair nevus accompanied by a linear nevus of the skin, and (3) woolly hair nevus acquired in adult life, in which the hair of the scalp assumes the characteristics of pubic hair.

A family history of similar abnormalities was not obtained in any of these cases. This is in distinct opposition to many well-documented families that show a long history of woolly hair of the entire scalp. Woolly hair of the entire scalp constitutes a separate entity.

622 W. 168th St.

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# A Critical Evaluation of the Effect of Steroid Lotions on Inflammatory Dermatoses

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Topical steroid therapy is widely used by physicians in the treatment of inflammatory dermatoses, and numerous ointments, creams, and lotions containing various steroids are today commercially available. So popular are these medications that an attempt was made recently to permit their over-the-counter sale.[1,2]

In studying the effect of drugs in the treatment of disease, many techniques have been developed to improve investigative methods. Crissey has emphasized the need for proper controls and evaluation of results in dermatologic therapy.[3] The effect of topical steroids has been studied by many dermatologists, and in many of the published reports the paired-comparison method has been used. In their original paper on the method, Sulzberger and his co-workers[4] stated: "It has been estimated that the results of such uniform symmetrical simultaneous paired comparison tests conducted in six men are as valid as an experiment using 50 men in whom non-symmetrical lesions are treated in rotation." However, additional safeguards of experimental design, such as double-blind technique, use of controls (placebos) as unknowns, randomization by the use of more than two agents to minimize chance of detection of the placebo, and mathematical analysis and validation of the results of the study, have been used in only a few such reports or not at all.

A review of the literature reveals no studies on topical steroids in which any attempt was made to analyse the results of treatment by biostatistical methods. In many, one steroid was compared with another without placebo control, and in only four was the double-blind method used. Three of these, by the Robinson and coworkers, appear to deal with the same groups of cases. In the first report[5] paired comparison studies were conducted on thirty hospitalized patients with generalized atopic dermatitis by members of the house staff under the supervision of the authors. "Four or more preparations were labelled by number and furnished as unknowns to the house officer." No difference in effect of the various steroids was noted, and no mention was made of the effect of the control base. The second report[6] states that paired comparison studies were "used primarily on hospitalized cases . . . . The preparations were furnished to the house officers with code number labels. The key to the code was kept by the secretary and was not revealed to either house officer or senior investigator until the study was complete." In usage studies, placebo and various steroids were used successively and "were substituted without the patient's or physician's knowledge." With this excellent experimental plan, it is unfortunate that one searches in vain for a statement of ef-

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fectiveness of placebo, to compare with the 94% to 31% effectiveness of the various steroids used and with the 100% to 84% effectiveness of the steroids in various dermatoses. In the third report,[7] only five patients were studied double-blind, and no statement of results is given. Eskind and co-workers[8] compared placebo base and hydrocortisone lotion, ointment, or cream by the double-blind method in 79 patients with Rhus dermatitis. No beneficial effect from the steroid was noted.

It has been shown that a single-blind study (in which only the patient is unaware of the identity of the medication he is receiving) is open to serious bias, which may be obviated by the double-blind method (in which neither the patient nor the evaluating physician knows what medication is being used). In discussing the measurement of subjective responses, Beecher[9] states: "It is essential that these (questions) be framed with care and posed in a neutral manner.... True neutrality cannot be preserved when any active participant in the experiment is aware of *when* an agent is tested or *what* that agent is. . . . Investigator's enthusiasm or bias comes out in subtle ways that are hard to detect at the time." It has been shown also that a difference between the effects of two medications does not necessarily indicate that one is superior to the other. Even if the two groups are similar in every respect except for the therapy, chance alone may explain the difference.[10] The science of biostatistics provides methods to determine the probability that chance alone may have caused the observed difference in results. Other safeguards are available to prevent bias in selection of patients.[11] It is our measured opinion that an investigator is obligated to take every possible precaution and to use every available means to ensure to as great an extent as possible the validity of his conclusions. These precepts were kept in the forefront of our minds throughout this study.

We have attempted to compare, by the double-blind paired-comparison method[4] the effect on inflammatory dermatoses of the preparations listed in Table 1. All of these were received from the pharmaceutical house in labeled 15 cc. flexible plastic vials.* Utilizing lists of randomly selected numbers, the project clerk numbered each vial individually with a different two-, three-, or four-digit number; removed the identifying label, and fastened each pair of vials together with cellophane tape. The three steroid preparations and the control base were randomized. The dispensing physician did not know, when he gave a pair of vials to his patient, whether each vial contained a steroid or whether one had steroid and the other had the base only. Therefore, one might even call this a triple-blind study, in that the physician could readily accept the fact that some patients would show equal effect in the two treated areas, and others, different effects. The coded paired vials were distributed to the nine dermatologists who participated in the study, for use in their offices, as well as in the Dermatology Clinics of the Northern and Southern Divisions of the Albert Einstein Medical Center.

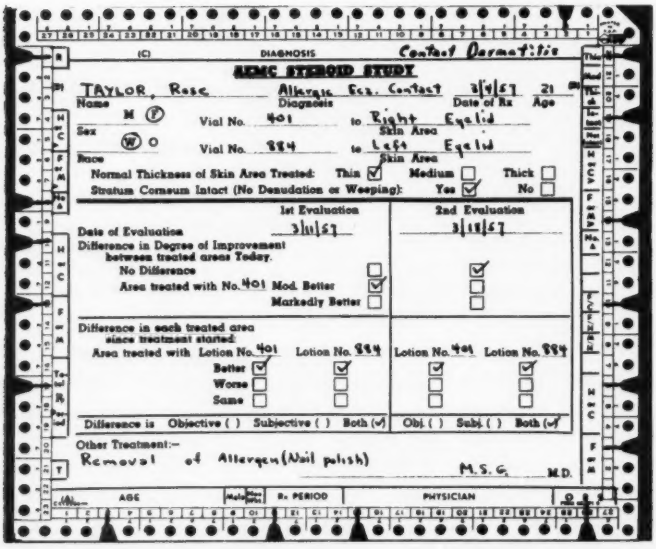
TABLE 1.—*Double-Blind Paired-Comparison Studies*

| | Abbrev. | Patients, No. |
|---|---|---|
| 0.1% fludrocortisone lotion vs. control lotion base * | F vs. C | 177 |
| 0.1% fludrocortisone lotion vs. 1.0% hydrocortisone lotion | F vs. H | 217 |
| 1.0% prednisolone lotion vs. 1.0% hydrocortisone lotion | P vs. H | 116 |
| Total | | 510 |

* The lotion base is an oil-in-water dispersable emulsion containing Ceramol (a carbowax), diglycol stearate, liquid petrolatum, glycerin, 6.5% isopropyl alcohol, and 0.15% methylparaben.

All patients with inflammatory dermatoses were eligible for inclusion in the study provided that more than one lesion was present and that the lesions were distributed fairly symmetrically. The patient was usually advised that two different strengths of the lotion were being tested to determine the optimal concentration for his condition, and he was instructed to apply each lotion (identified only by an individual code number) sparingly to the designated area three times a day and rub

* Merck Sharpe & Dohme, Division of Merck & Co., Inc., supplied the materials used and gave financial assistance in this study.



(C) DIAGNOSIS Contact Dermatitis

ARMC STEROID STUDY

Name TAYLOR, Rose — Diagnosis Allergic Eczematous Contact — Date of Rx 3/9/57 — Age 21

Sex M (P) — Vial No. 401 to Right Eyelid Skin Area

Race (W) O — Vial No. 884 to Left Eyelid Skin Area

Normal Thickness of Skin Area Treated: Thin ☑ Medium ☐ Thick ☐

Stratum Corneum Intact (No Denudation or Weeping): Yes ☑ No ☐

| | 1st Evaluation | 2nd Evaluation |
|---|---|---|
| Date of Evaluation | 3/11/57 | 3/18/57 |
| Difference in Degree of Improvement between treated areas Today. | | |
| No Difference | ☐ | ☑ |
| Area treated with No. 401 Mod. Better | ☑ | ☐ |
| Markedly Better | ☐ | ☐ |
| Difference in each treated area since treatment started: | | |
| Area treated with | Lotion No. 401 / Lotion No. 884 | Lotion No. 401 / Lotion No. 884 |
| Better | ☑ / ☑ | ☑ / ☑ |
| Worse | ☐ / ☐ | ☐ / ☐ |
| Same | ☐ / ☐ | ☐ / ☐ |
| Difference is | Objective ( ) Subjective ( ) Both (✓) | Obj. ( ) Subj. ( ) Both (✓) |

Other Treatment:— Removal of Allergen (Nail polish)

M.S.G. M.D.

AGE — Mo. Day Yr. — Rx. PERIOD — PHYSICIAN

Figure 1

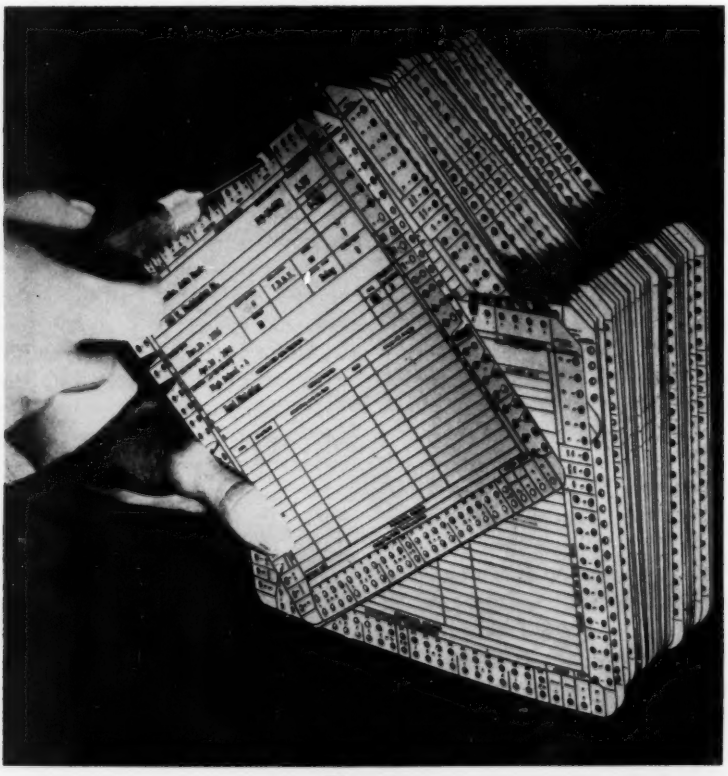


Figure 2

in well. He was usually asked to return for evaluation in one week. A specially devised form, printed on McBee Keysort punched card † (Fig. 1) was utilized for entering data, for marginal punching, and for analysis of results. These cards have been used to advantage in other medical studies.[12] The upper third of the card was completed by the physician at the time the lotions were given the patient (above the double line in Fig. 1). At the time of evaluation, the lower section was completed. If a subsequent evaluation was carried out, this also was entered. The cards were then collected and returned to the clerk, who consulted her list of random numbers and entered on the card the name of the preparation used. She then punched the marginal holes of the cards in accord with the printed coding opposite them (Fig. 1). Diagnoses were punched at the top; age, sex, race, duration of treatment, and evaluating physician, at the bottom; character of skin and results of first evaluation, on the right, and results of second evaluation, on the left. The punch cuts off the external border of the hole, so that on sorting by inserting a knitting needle in a given hole, cards with a punched hole fall and those with an unpunched hole remain suspended by the needle (Fig. 2).

† The McBee Company, 1041 Hamilton St., Allentown, Pa.

Five hundred forty-two patients were treated in this study. However, the cards of 32 were discarded before statistical analysis because their diagnoses were considered not responsive to topical steroid therapy. These diagnoses are acne neurotica; alopecia areata; amyloidosis, localized; blastomycosis; dermatitis herpetiformis; dermatitis medicamentosa; erythema annulare centrifugum; erythema multiforme; folliculitis; Fox Fordyce disease; granuloma annulare; keratosis palmaris; lichen amyloidosis; papular urticaria; poikiloderma vasculare atrophicans; pityriasis rosea, and sycosis vulgaris. Thus, 510 patients were available for analysis.

An attempt was made to measure the response of each skin area to treatment, both in relation to the response of the other treated area, and to its condition before treatment. The difference *between* the two treated areas *at the time of evalua-*

TABLE 2.—*One Hundred Seventy-Seven Patients in Whom Fludrocortisone Lotion (F) Was Compared with the Control Lotion Base (C) by the Double-Blind Paired-Comparison Method*
Analysis of Results by Diagnosis

| | Difference Between the 2 Treated Areas * | | | | | Change in Each Area Since Start of Treatment † | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | F | | | C | | |
| Diagnostic Classification | F++ | F+ | ND | C+ | C++ | Total | Better | Same | Worse | Better | Same | Worse |
| Atopic dermatitis | 4 | 5 | 13 | 3 | 0 | 25 | 20 | 3 | 2 | 18 | 5 | 2 |
| Contact dermatitis | 4 | 12 | 18 | 4 | 0 | 38 | 31 | 5 | 2 | 25 | 10 | 3 |
| Eczematous dermatitis | 0 | 2 | 3 | 0 | 0 | 5 | 3 | 1 | 1 | 2 | 1 | 2 |
| Erythroderma, generalized, & exfoliative dermatitis | 0 | 1 | 1 | 0 | 0 | 2 | 1 | 1 | 0 | 1 | 1 | 0 |
| Hand eruptions, eczematous | 2 | 1 | 6 | 0 | 0 | 9 | 8 | 1 | 0 | 6 | 3 | 0 |
| Hyperhidrosis & hyperidrotic dermatitis | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 |
| Infectious eczematous dermatitis | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 0 |
| Intertrigo & intertriginous moniliasis | 1 | 1 | 5 | 3 | 1 | 11 | 7 | 4 | 0 | 8 | 3 | 0 |
| Lichen simplex chronicus (localized neurodermatitis) | 2 | 5 | 16 | 4 | 0 | 27 | 19 | 8 | 0 | 17 | 9 | 1 |
| Miliaria | 3 | 1 | 3 | 1 | 0 | 8 | 8 | 0 | 0 | 4 | 4 | 0 |
| Neurodermatitis, generalized | 0 | 2 | 7 | 2 | 0 | 11 | 9 | 1 | 1 | 8 | 2 | 1 |
| Nummular eczema | 1 | 1 | 6 | 1 | 1 | 10 | 8 | 2 | 0 | 8 | 2 | 0 |
| Psoriasis | 0 | 0 | 1 | 1 | 0 | 2 | 1 | 1 | 0 | 2 | 0 | 0 |
| Seborrheic dermatitis | 1 | 3 | 7 | 2 | 1 | 14 | 12 | 2 | 0 | 11 | 3 | 0 |
| Stasis dermatitis | 0 | 1 | 3 | 0 | 0 | 4 | 4 | 0 | 0 | 4 | 0 | 0 |
| Miscellaneous ‡ | 0 | 1 | 6 | 0 | 2 | 9 | 7 | 2 | 0 | 8 | 1 | 0 |
| Total | 19 | 36 | 96 | 21 | 5 | 177 | 139 | 31 | 7 | 122 | 45 | 10 |

* ++, markedly better than opposite side; +, moderately better than opposite side; ND, no difference between the two treated areas
† Better, same, worse relate to comparison with pretreatment status.
‡ Acrodermatitis continue; Hailey-Hailey disease; insect bite reactions; light sensitivity; perleche; pruritus scroti, vulvae, ani; rosacea and acne rosacea; senile pruritus; tinea cruris.

TABLE 3.—*One Hundred Seventy-Seven Patients in Whom Fludrocortisone Lotion (F) Was Compared with the Control Lotion Base (C) by the Double-Blind Paired-Comparison Method*
Analysis of Results by Sex, Skin Thickness, and Status of Stratum Corneum

| | Difference Between the 2 Treated Areas * | | | | | F | | | C | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | F++ | F+ | ND | C+ | C++ | Total | Better † | Same | Worse | Better | Same | Worse |
| Sex | | | | | | | | | | | | |
| Male | 7 | 11 | 43 | 11 | 4 | 76 | 58 | 14 | 4 | 54 | 18 | 4 |
| Female | 12 | 25 | 53 | 10 | 1 | 101 | 81 | 17 | 3 | 68 | 27 | 6 |
| Skin thickness | | | | | | | | | | | | |
| Thin | 5 | 8 | 18 | 9 | 1 | 41 | 29 | 11 | 1 | 25 | 14 | 2 |
| Medium | 10 | 20 | 53 | 8 | 3 | 94 | 78 | 11 | 5 | 69 | 19 | 6 |
| Thick | 0 | 1 | 2 | 1 | 0 | 4 | 3 | 1 | 0 | 3 | 1 | 0 |
| Not specified | 4 | 7 | 23 | 3 | 1 | 38 | 29 | 8 | 1 | 25 | 11 | 2 |
| Stratum corneum | | | | | | | | | | | | |
| Intact | 10 | 20 | 55 | 13 | 3 | 101 | 80 | 16 | 5 | 72 | 24 | 5 |
| Not intact | 2 | 5 | 13 | 2 | 1 | 23 | 18 | 4 | 1 | 16 | 4 | 3 |
| Not specified | 7 | 11 | 28 | 6 | 1 | 53 | 41 | 11 | 1 | 34 | 17 | 2 |
| Total | 19 | 36 | 96 | 21 | 5 | 177 | 139 | 31 | 7 | 122 | 45 | 10 |

*++, markedly better than opposite side; +, moderately better than opposite side; ND, no difference between the two treated areas.

† Better, same, and worse relate to comparison with pretreatment status.

*tion* demonstrated the difference in effect, if any, between the two agents employed. The change in *each* area *since the start of treatment* demonstrated the effect of each agent on the treated site.

Table 2 presents a breakdown by diagnosis, and Table 3, by sex, skin thickness, and status of the stratum corneum of the 177 patients in whom a comparison of fludrocortisone lotion and control lotion base was made (F vs. C). The difference *between* the two treated areas is shown on the left; the difference in *each* area since start of treatment, on the right. Analysis by age is not presented, as it revealed nothing of significance. Table 4 relates the changes in each area in the individual patient. It may be noted that in the 10 patients in whom the C-treated area was worse after treatment, in 3 the F-treated area was improved; in 7, worse. All 10 of these patients had atopic, contact, eczematous, or neurodermatitis. Of the 122 patients in whom the C-treated area was improved on treatment, the F-treated area was improved in 112, the same in 10, and worse in none. Table 5 presents in summary the over-all findings in the F vs. H (fludrocortisone vs. hydrocortisone) and P vs. H (prednisolone vs. hydrocortisone) groups. In these groups, both areas were worse after treatment in 10 patients, and in 1 patient one area was better and one was worse. There was nothing distinctive about the diagnoses of these 11 patients.

Inasmuch as no standard formula was found in the available references for analyzing data of this type, several theoretical problems remained to be solved. The first of these concerned the question of how to handle statistically the patients who exhibited no difference in response to the two preparations. The second dealt with the difficulty in evaluating observations of differences described as "moderately better" and "markedly better."

A solution to each of these problems was developed, and the figures for the F and C preparations presented in Table 2 are analyzed in another paper.[13] The conclusion reached was that the observed data did not

TABLE 4.—*Comparison of Results with the Two Lotions on the Same Patients* *

| | F Better | F Same | F Worse | Total |
|---|---|---|---|---|
| C better | 112 | 10 | 0 | 122 |
| C same | 24 | 21 | 0 | 45 |
| C worse | 3 | 0 | 7 | 10 |
| | 139 | 31 | 7 | 177 |

* See Table 2 for details.

TABLE 5.—*Summary of Results of Testing Lotions Containing Fludrocortisone and Prednisolone Against Hydrocortisone* *

| | | | | | | | F | | | H | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | F++ | F+ | ND | H+ | H++ | Total | Better | Same | Worse | Better | Same | Worse |
| F vs. H | 8 | 43 | 117 | 38 | 11 | 217 | 171 | 38 | 8 | 164 | 46 | 7 |
| | | | | | | | P | | | H | | |
| | P++ | P+ | ND | H+ | H++ | Total | Better | Same | Worse | Better | Same | Worse |
| P vs. H | 1 | 12 | 84 | 17 | 2 | 116 | 98 | 16 | 2 | 97 | 15 | 4 |

* See Table 1 for details.

F, fludrocortisone; H, hydrocortisone; P, prednisolone; ++, markedly better than opposite side; +, moderately better than opposite side; ND, no difference between two treated areas; better, same, and worse relate to comparsion with pretreatment status

demonstrate any differences statistically significant at the 5% level (the generally accepted standard employed in therapeutic research). No significant difference was found in either sex, in any diagnotic group, between areas of different skin thickness, or in comparing areas with and without an intact stratum corneum (Tables 2 and 3). In addition, none of the three steroid lotions studied proved superior to the others (Table 5) when submitted to statistical analysis.

## Comment

We were startled to find no significant difference between the effect of steroid and that of the control base in this study. Almost every dermatologist will attest to the dramatic effectiveness of topical steroid therapy in many patients. In addition, many studies in the literature conclude that such treatment is effective. How then can we explain our findings? Batterman and Grossman [14] were also surprised when they found a known effective analgestic (acetylsalicylic acid), a placebo, and an unknown drug of equal value in relief of pain of osteoarthritis and related conditions when studied by the double-blind method. They state: "There appears to be an incidence of effectiveness that occurs with all medicaments with the double blindfold technique, regardless of what preparations are investigated." They conclude that this technique is of no value in evaluating long-term therapy.

The effect of placebo on a variety of diseases and symptoms has been intensively studied in recent years.[9-11,14-34] That it may have marked beneficial action (as well as side-effects) (Wolf and Pinsky [15]) has been shown beyond doubt. How can an inert substance cause such objective as well as subjective changes? Wolf [16] states: "That 'placebo effects' occur depends . . . on [the fact that] the mechanisms of the human body are capable of reacting not only to direct physical and chemical stimulation, but also to symbolic stimuli, words and events which have somehow acquired special meaning for the individual. . . . The pharmacologic action of an agent may be outweighed [by placebo effect] and its effect thus reversed." Wolff [17] says: "The placebo is a symbol of the doctor saying in effect, 'I will take care of you'." Russek [18] says: "The pill the patient swallows, no matter what its nature, acquires potency as a symbol of faith, wisdom, and support." Beecher [19] states that there are two phases in suffering pain, the original pain sensation and then the reaction to it (processing of pain) by the central nervous system. He believes that placebo influences the second phase. An identical statement can be made regarding itching.

Beecher [19] analyzed 15 unselected published double-blind studies involving controls, in each of which an attempt was made to evaluate treatment of one of a variety of symptoms (cough, severe postoperative

pain, angina pectoris, headache, seasickness, common cold, etc.). Over 1000 patients were studied. Placebo was found effective in 35.2±2.2%. Beecher then comments: "With placebos having an average high effectiveness of 35% . . ., it should be apparent that 'clinical impression' is hardly a dependable source of information. Many 'effective' drugs have power only a little greater than that of a placebo. . . . To separate out even fairly great true effects above those of a placebo is manifestly difficult to impossible on the basis of clinical impression. Many a drug has been extolled on the basis of clinical impression when the only power it had was that of a placebo."

It has been suggested to us that the improvement seen at the site of application of the control base in many of our patients may have resulted from transcutaneous absorption of the steroid from the steroid-lotion-treated site and subsequent transportation via the blood stream to the control-treated site. The entire vial of steroid lotion (15 cc. of 0.1% concentration) contains only 15 mg. of fludrocortisone. If entirely used within a week, 2 mg. would be applied topically each day. Livingood et al.[35] demonstrated systemic absorption of topically applied fludrocortisone lotion when this was applied in amounts ranging from 4 to 60 mg. per day, but he gave no data on the amount absorbed. It appears unlikely to us that enough of the 2 mg. of steroid applied per day at one site could be absorbed and transmitted via the blood stream to a distant site to cause equal anti-inflammatory effect at the two sites.

We believe that the following factors explain our inability to demonstrate superiority of steroid over control base in this study.

1. Lasagna and his co-workers[22] have demonstrated that placebo reactors are a more anxious, self-centred, emotionally labile, dependent, and immature group than are nonreactors, who are more rigid and emotionally controlled. They point out that neither group can be considered normal emotionally. An editorial in *The Journal of the American Medical Association*[23] states: "A large number of [placebo] reactors in the control series [of a double-blind test] would tend to decrease the difference between the results obtained with a potent and valuable drug and the controls, possibly to the point of indicating that the drug was worthless." It is probable that many of our patients were placebo reactors and that this explains in part not only the lack of significant superiority of the steroid over the base but also the large per cent of patients (54.8%) in whom the two were equal in effect. Similarly, in a number of reports in the literature, a large percentage of the patients showed equal effect from two steroids applied topically in paired-comparison studies. In addition, in purely therapeutic paired-comparison studies in his office, one of us (I. L. S.) has been impressed with the frequency of similar effect of two very different topical agents.

2. The editorial referred to above[23] states: ". . . it is difficult to evaluate the effect of drugs on a disease in which a large psychosomatic factor is present. . . ." Most dermatologists agree that the psyche plays an important role in many inflammatory dermatoses.

3. Topical steroid treatment is effective in a limited number of dermatologic patients, this effectiveness depending not only on the diagnosis but also on the degree of inflammation, the location, and probably other factors. Dingle and co-workers[36] found that only 1.5% of over 1000 patients with respiratory diseases had infections which were bacterial in origin. Israel[37] has pointed out that if all of these patients had been treated with penicillin (a not inconceivable circumstance in the practice of medicine today) a controlled study of this group would show no benefit from the antibiotic. The effectiveness of the treatment in the few patients with bacterial infections susceptible to such therapy would be masked by the large number with conditions not amenable to this treatment. Similarly, we believe that in the

essentially unselected group of patients in this study, the large number of dermatoses unaffected by steroids obscured the few benefited. Pruritis ani, vulvae, and scroti are relatively common and usually respond well to topical steroid treatment. Because our study was limited to paired comparison, only three patients with these complaints were treated in the F vs. C group. Thus, the conditions of our experiment made it necessary to exclude many patients whom the treatment would be expected to benefit.

We believe these to be the major factors. Minor factors are the following.

4. A lotion base which contains a small amount of isopropyl alcohol was used. Many acute dermatoses require the emollient effect of an ointment. The irritant effect of the alcoholic lotion may have overshadowed any beneficial steroid effect.

5. As only 15 cc. of the lotion was available for treatment of each area, the amount may have been insufficient to bring about improvement in some patients.

6. Although we were unable to demonstrate greater efficacy in areas of thin skin and in dermatoses in which the stratum corneum was not intact, it is believed that poor penetration of the steroid through thick intact skin may have prevented demonstrable benefit in some patients.

7. Lotions containing only inert agents are known to have an antipruritic effect, due to cooling by evaporation and protection by the powder. Objective improvement, evidenced by diminution in erythema, excoriations, and lichenification may have occurred in the control area as a result of relief of pruritus, thus obscuring the beneficial effect of the steroid. In other words, the control lotion base was not a pure placebo, in that it was effective through its cooling and protective action.

## Summary

The double-blind paired-comparison method was used in studying the effect of three steroid lotions and a control lotion in 510 patients with inflammatory dermatoses.

A newly devised statistical method was employed which utilizes the large percentage of patients in whom there was no difference in effect and which weights degree of difference of response to the two agents studied.

In 177 patients in whom 0.1% fludrocortisone lotion was compared with control lotion base, no statistically significant difference in effect could be demonstrated.

Analysis by age, sex, diagnosis, skin thickness, and presence or absence of stratum corneum in dermatitic areas revealed no group in which there was a significant benefit from the steroid lotion as compared with the control lotion.

No significant difference was found in 217 patients between the effect of 0.1% fludrocortisone lotion and 1.0% hydrocortisone lotion nor in 116 patients between 1.0% hydrocortisone lotion and 1.0% prednisolone lotion.

An attempt is made to explain the discrepancy between the findings in this study and the experience of most dermatologists.

## Conclusions

The placebo reactor is an important potential source of error in studies of the effect of therapeutic agents.

Topical steroid therapy, while dramatically effective in certain dermatologic patients, has not been shown, under the conditions of this study, to be superior to control base in a wide variety of cases which were not critically selected. The experienced dermatologist has learned when and when not to treat with steroids. That they are not usually effective when used indiscriminately is demonstrated by this study.

Drs. Milton Cahn, Edwin Levy, Albert Order, Reuben Schwartz, Bertram Shaffer, David Sidlick, and Jack Weiner, of the Dermatology Staff of the Albert Einstein Medical Center, clinically evaluated the results of treatment in many of the patients in this study.

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# On the Evaluation of Paired Comparison Studies

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In the clinical testing of new therapeutic measures, dermatologists often have the opportunity of planning their study in such a way that the individual patient may serve as his own control. By applying the blank control base and the preparation containing the locally acting medicament to comparable areas of the body surface, the investigator can minimize the difficulties caused by the high variability of response in different patients.[1]

By subjecting to statistical analysis the difference in response to the new drug versus the control at symmetrical sites on the same patient, one may expect a significant difference to appear with fewer trials than if the experimental therapy and the control were employed in different persons.[2] Of course, the double-blind method, utilizing a properly randomized coding scheme, is of the utmost importance, so that neither the patient nor the examining physician will be biased in evaluating the results being compared. The tacit assumption is made that the medication applied locally has no appreciable effect upon the symmetrically located lesion.

In a carefully planned project, Schamberg, Askovitz, and Greenberg [3] attempted to evaluate objectively several topical steroid preparations. A double-blind procedure was used, with the lotion containers identified only by a numbered label. Over 500 patients were included in the study, and the observations were recorded on a specially designed Keysort punched card.

Two interesting problems arose in the mathematical analysis of the resulting figures. When a search of the recent literature did not reveal any preferred approach, a fairly straightforward method was developed for handling the data in this type of investigation. These concepts are being presented here in the hope that they may be of interest to other workers in the field of therapeutic research.

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## The "No Difference" Response

The first question was whether to include the number of patients in whom no difference was observed between the response to the experimental preparation and to the control base. To omit these patients from the calculations altogether did not seem proper, if the aim of the investigation is to estimate the value of the new product under conditions of actual practice. Perhaps an exaggerated example may clarify the point.

Let us assume that a new therapeutic agent (together with a control) has been tried in 20 patients having a specific disorder and that in 19 of the patients the new drug elicited a better response than did the control. In one patient the control was judged to have been more effective than the drug. The success rate of the new product might then be taken as 19 out of 20, and the new agent would no doubt be seized upon as a definite therapeutic advance.

In keeping with the standard practices of statistical evaluation, the mathematical details may be stated as follows: If the new drug and the control were actually of equal effectiveness, and in the complete absence of bias, we would expect "on the average" that for 10 patients there would be a report of a better response at the site which had received the treatment and for the remaining 10, a better response in the area which had received the control. (It is assumed that a definite statement in favor of one area

or the other must be made for each patient.) However, we would not be taken by surprise if in another series of 20 patients the reported figures in favor of treatment and control were 11 and 9, respectively, or 12 and 8. How large a discrepancy from the average result of 10 and 10 is to be accepted as within the realm of chance variation?

Here the theory of probability has been applied. Abstractly, there is no difference whether we consider the outcome of two equally effective treatments in dermatologic patients or the likelihood of obtaining heads or tails in coin tossing. Now, on tossing an unbiased coin 20 times, the probability of obtaining 19 heads and 1 tail is [4] less than 1 in 52,000—"extremely unlikely." If this did take place, we would be inclined to view with suspicion the assumption that the coin was unbiased and subject to no influence other than chance. Similarly, we would reject the "null hypothesis" that treatment and control are equally effective, since the observed outcome was so unlikely to occur under that assumption.

In general, if a series of observed results has a likelihood of happening, on the basis of a null hypothesis, less than once in 20 times, it is customary to reject chance alone as a satisfactory explanation. In this case, we would state that treatment and control are "significantly different at the 5% level." More exact standards are infrequently used in medical investigations. Occasionally, the 1% level is used to establish a "highly significant" difference, if the observed events had less than 1 chance in a 100 to occur under the null hypothesis.

Returning to the paired comparison study, let us now assume that the new method of treatment had been tried in a series of 100 patients and that the results were as follows: New treatment definitely better than control, 19 patients; new treatment inferior to control, 1 patient, and no difference between new treatment and control, 80 patients.

If we were to eliminate the 80 patients in whom the new therapy was no better than the control, the ratio of 19:1 might give a rather distorted view of the actual observations. Certainly some consideration should be given to the 80% in whom the new treatment had shown no advantage over the control treatment.

As a more extreme example, let us now assume that the new therapeutic agent had been tested in 1000 patients. If the final data showed that 19 patients benefited more by the new drugs than by the control; 1 patient, less, and 980, with equal effect, we would hardly be expected to ignore the fact that the new product was no more effective than the control in 98% of the patients on whom it was tried.

In an attempt to overcome this difficulty, it was decided to divide the number of patients in whom no difference was observed into two equal groups and to add the number in each group to the totals of patients in whom there had been an observed difference. To express this more simply, the use of algebraic symbols may serve to advantage.* Let $T$ represent the number of patients for whom the new treatment proved superior to the control; $C$, the number of persons for whom the control application was found superior to the new treatment, and $ND$, the number in whom no difference was noted between treatment and control.

Instead of inquiring whether the numbers $T$ and $C$ are significantly different or not, let us consider instead the modified figures $T'=T+\frac{1}{2}ND$ and $C'=C+\frac{1}{2}ND$. This method has the advantage that it does not ignore $ND$, nor does it unduly influence evaluation of the superiority of either treatment or control.

Returning to the analysis of the hypothetical results given previously, let us take up first the case of $T=19$, $C=1$, $ND=80$. Is the larger value of $T$ a genuine indication of the effectiveness of the treatment, or is it merely a chance variation that might be observed even if the treatment were actually of no value? If treatment and control had been administered to 100 patients and the two were known to be equally effective, we

* All symbols used in this paper are defined in the Table (p. 503).

would not be in a position to make any prediction concerning the average $T$ or $C$ value unless we had some information regarding the frequency of the $ND$ response. For example, if we had reason to expect an $ND$ value of about 40, then we could predict average $T$ and $C$ values of 30 each.

However, regardless of how large or small $ND$ is, it can still be stated that if the treatment is ineffective we may expect in the long run that $T'=C'$, except for chance fluctuations. Thus, for a series of 100 patients, the average expected result with the null hypothesis would be $T'=50$, $C'=50$, even though we cannot predict any expected value for $T$ or $C$ with which to compare the observed $T$ and $C$.

Now, how large a discrepancy between the observed $T'$ and $C'$ is considered within the realm of fortuitous variation? The theory of probability provides us with an answer. Taking the 5% level of significance generally employed in medical research, it is agreed to accept an outcome of an experimental trial as statistical evidence if the result would occur under the null hypothesis less than 5 times in 100 repeated trials.

Although various techniques of calculation are available, perhaps the simplest method of obtaining an answer is to consult published tables [6,7] of "minimum contrast." In the manual by Mainland and associates,[7] for $N=100$ (the number of patients studied), we find that a significant difference from $T'=50$ and $C'=50$ would require (at the 5% level) a minimum experimental $T'$ of 61. In the example above, T' is only 59. Therefore, the data do not offer evidence of the superiority of the treatment according to conventional standards.

### Weighting of Responses

The other problem which arose was how to evaluate equitably statements such as "steroid treated skin area is 'moderately better' than control area," as compared with "steroid treated area is 'markedly better' than control area." Several possibilities exist. At one extreme, we might assign equal importance to each of the above observations. This amounts to taking the evidence in favor of the new therapy given by a result of "moderately better" to be just as great as from the result stated "markedly better." Under this assumption, we would merely add together the total number of patients for whom the treated area was better to any degree, "markedly" or "moderately," and continue the analysis from there. At the opposite extreme, it might be considered proper to ignore completely a "moderately better" response as evidence in favor of the treatment.

A third possibility, and perhaps the most impartial of all, would be to weight the evidence of a "moderately better" response as less important than "markedly better" but not to disregard it altogether. If a "moderately better" result has only the fraction $f$ of the value of a response of "markedly better," then we may proceed as follows.

Let $T++$ represent the number of patients for whom the area receiving the steroid proved to give a "markedly better" result than the corresponding area receiving the control base, and let $T+$ similarly stand for the number of patients in whom the steroid-treated area was "moderately better" than the control area. Then the total number of "patient-units" of evidence in favor of $T$ would be given by

$$T^*=(T++)+f(T+)$$

and

$$C^*=(C++)+f(C+)$$

The number remaining when $T$ and $C$ are subtracted from the total number of patients included in the study would provide the revised $ND$. Or

$$ND^*=ND+(1-f)(T+)+(1-f)(C+)$$

Now, having given due consideration to the difference in weight between "markedly" and "moderately" better, we may proceed to evaluate the presence or absence of an over-all significant result. For this purpose, we calculate $T'=T^*+\frac{1}{2}ND^*$, and $C'=C^*+\frac{1}{2}ND^*$, and proceed as previously.

All symbols used in this paper are defined in the Table (p. 503).

*Symbols and Formulas Used in Evaluation of Paired Comparison Studies*

| Symbol | Explanation |
|---|---|
| $C$ | The number of patients in whom the result at the control area was superior to that obtained with the experimental treatment |
| $T$ | The number of patients in whom the result observed with the therapeutic agent being tried was superior to that obtained at the control site |
| $ND$ | The number of patients in whom no clinical difference was observed between the two areas |
| $C+$ | The number of patients in whom the result with the control was judged "moderately better" than with the new treatment |
| $C++$ | The number of patients in whom the result with the control was stated to be "markedly better" |
| $T+$ | The number of patients with a "moderately better" result at the area receiving the new therapeutic agent, in comparison with the control |
| $T++$ | The number of patients with a "markedly better" result observed at the treated site |
| $f$ | The fraction indicating the relative weight of a + observation as compared with a ++ difference |
| $C^*$ | The number of patient-units of evidence in favor of the control, after adjustment for the reduced value of the "moderately better" results as evidence |
| $T^*$ | The number of patient-units of evidence favoring the new therapeutic agent, after the reduced weight of the "moderately better" responses is taken into account |
| $ND^*$ | The total number of patient-units providing no evidence in favor of either control or new treatment |
| $C'$ | The adjusted number of patient-units favoring the control, after the equitable division of the "no difference" results |
| $T'$ | The adjusted number of patient-units in favor of the trial treatment after the "no difference" total has been equally assigned |

Formulas †

$$C^* = (C++)+f(C+) \quad (1)$$
$$T^* = (T++)+f(T+) \quad (2)$$
$$ND^* = ND+(1-f)(C+)+(1-f)(T+) \quad (3)$$
$$C' = C^*+\tfrac{1}{2}ND^* \quad (4)$$
$$T' = T^*+\tfrac{1}{2}ND^* \quad (5)$$
$$C' = C+\tfrac{1}{2}ND \quad (6)$$
$$T' = T+\tfrac{1}{2}ND \quad (7)$$

† Formulas 1 to 5 apply where both "moderately better" and "markedly better" degrees of difference are considered. Formulas 6 and 7 apply where only a single type of response is permitted. In either case, $C'$ and $T'$ are the values subjected to statistical analysis to determine whether a significant difference exists.

## Example

The principles outlined above are easy to apply to actual data. In the study on steroid lotions, the results obtained in comparison between fluorohydrocortisone and control lotion were as follows: $T++=19$, $T+=36$, $ND=96$, $C+=21$, $C++=5$. It was the opinion of the dermatologists carrying out the study that a single patient in whom one treated area was "markedly better" than the other was approximately equivalent, as evidence for the superiority of the treatment applied to that area, to four patients in whom this area was "moderately better" than the other. Therefore, the value of ¼ was taken for the fraction $f$. The calculations are then as follows:

$T^*=(T++)+\frac{1}{4}(T+)=19+\frac{1}{4}(36)=19+9=28$
$C^*=(C++)+\frac{1}{4}(C+)=5+\frac{1}{4}(21)=5+5.25=10.25$
$ND^*=ND+\frac{3}{4}(T+)+\frac{3}{4}(C+)=96+\frac{3}{4}(36)+\frac{3}{4}(21)$
$=96+27+15.75=138.75$
$T'=T^*+\frac{1}{2}ND^*=28+\frac{1}{2}(138.75)=28+69.37=97.37$
$C'=C^*+\frac{1}{2}ND^*=10.25+\frac{1}{2}(138.75)=10.25+69.37=79.62$

By reference to the Mainland tables,[7] this difference between $T'$ and $C'$ is not significant at the 5% level.

## Summary

Two problems commonly arising in evaluating the results of paired comparison testing of therapeutic agents are discussed. Simple solutions are offered to the question of how to deal statistically with the number of patients in whom the response to the new drug is no different clinically from the response to treatment with a blank control and to the difficulty arising from varying degrees of difference in response to the agents studied.

4900 N. 9th St. (41).

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## Clinical Notes, New Instruments and Techniques

# Chlorothiazide in Acne

**FRANK E. CORMIA, M.D., New York**

In a recent study, Kalz and Scott[1] investigated some of the cutaneous changes during the menstrual cycle. They found that the skin, similarly to other body tissues, took on added water during the premenstrual period. On the basis of this finding, they employed an oral diuretic premenstrually in a series of patients with acne. The active ingredient of the diuretic was ammonium chloride, and the average daily dose was about 2 gm. They reported that this medication had a moderately good supressing effect on the premenstrual flare-ups of acne.

More recently, chlorothiazide (Diuril) has become available for clinical use. This drug is an exceptionally potent, orally effective, nonmercurial diuretic agent.[2] Accordingly, chlorothiazide was administered to a group of 20 patients who had severe premenstrual flare-ups of their acne. Most of these patients previously had been given conjugated estrogenic substances (Premarin) during the last portion of the menstrual cycle, with varying degrees of success. Chlorothiazide was administered in a dosage of 500 mg. twice daily for 10 days before the onset of the period and for 3 days thereafter. The results of the treatment were exceptionally good and were definitely superior to those obtained with conjugated estrogenic substances. Premenstrual exacerbations of acne were favorably influenced in every case and were completely suppressed in 18 cases. The only adverse reaction was a troublesome frequency of urination in one patient.

This report is not to be construed as a new treatment for acne; it is recommended only to prevent premenstrual exacerbations of acne.

1070 Park Ave. (28).

Submitted for publication May 17, 1958.

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# Dermatitis Medicamentosa Due to Diuril (Chlorothiazide)

*Report of Three Cases*

**JAMES R. ROGIN, M.D., Detroit**

During the past month three cases of skin eruption due to the ingestion of a new antihypertensive and diuretic drug, chlorothiazide, (Diuril, Merck) have been encountered. Since there have been no reports of cutaneous eruptions due to this drug, it was thought worth while to call attention to this complication of the use of a new drug which has recently attained wide popularity.

Submitted for publication June 10, 1958.

CASE 1.—A 37-year-old white woman, a physician's wife, was given chlorothiazide for premenstrual edema and congestion of the breasts. She took the drug in the dosage of 250 mg. twice daily for two days, a total of 1.0 gm. About eight days after the last dose was taken, she noted a pruritic eruption on her legs. Within a few days the eruption had spread from the toes to the groins and involved also the hands and arms from the fingers

to the axillae. This eruption was brightly erythematous and papular in character, with a few scattered, very small, papulovesicular lesions. The eruption was intensely pruritic and was accompanied by much edema of the ankles, lower legs, and hands. At no time during the course of the eruption did any lesions appear on the trunk. There was no history of ingestion of any other drug in addition to the chlorothiazide, and this, plus the symmetrical distribution of the eruption and its other clinical characteristics, was felt to be enough evidence that the eruption was due solely to the chlorothiazide.

The eruption persisted for two weeks, during which time treatment was given to relieve the pruritus with one of the antihistaminic drugs by mouth plus colloid baths and the p. r. n. application of an oily antipruritic lotion. By the end of two weeks, visible evidence of the eruption had disappeared, as had the edema of the hands, feet, and lower legs, although the patient still complained of some pruritus in the originally affected areas.

CASE 2.—A 62-year-old white woman, suffering from cardiac congestion and peripheral edema, was given chlorothiazide in the dosage of 250 mg. twice daily for 10 days, at which time a generalized erythematopapular eruption appeared on her trunk and extremities. In addition to the erythema and the papules, there were also many small purpuric lesions, which did not blanch on pressure. Although the patient had been taking other medications for her cardiac disorder, none of these was new to her, and she had been taking all of them for some months without difficulty. Her eruption appeared after she had taken chlorothiazide for a period of 10 days. The eruption disappeared completely two weeks after the chlorothiazide was discontinued, although her other medications were continued during this time. The purpuric lesions persisted for about three weeks after the generalized erythematopapular eruption had disappeared.

CASE 3.—A 42-year-old white woman had taken chlorothiazide rather irregularly for the past six months. Her physician had prescribed the drug for premenstrual edema and tension. The patient had taken the drug in the dosage of 500 mg. once daily for two or three days when she became aware of edema. She had no difficulty with the drug until the past month, when she took the chlorothiazide faithfully in the dosage of 500 mg. once daily for eight days. On the eighth day, she noted an erythematopapular pruritic eruption on the dorsal surface of her left forearm. Within 48 hours similar lesions appeared on both hands, her arms from wrists to axillae, around her neck and her legs from the toes to the groins. There were no lesions on her trunk at any time during the course of her eruption. The lesions on her extremities were accompanied by a great deal of edema of the feet, the lower legs and ankles, and the hands. The patient was taking no medication other than the chlorothiazide. Her pruritus was so severe that it was deemed advisable to treat her with triamcinolone, which was prescribed in the dosage of 4 mg. every 6 hours around the clock for 72 hours, after which the dosage was reduced to 4 mg. four times daily. When the patient was seen one week later, her visible dermatitis had faded a good deal but she was still greatly annoyed by severe pruritus sufficient enough that an antihistaminic drug was added to her therapeutic regimen. This patient is still under observation, and so the total duration of her eruption has not as yet been determined.

1150 Griswold Avenue (26).

### Addendum

Since the above report was submitted for publication, there has appeared in *J. A. M. A.* (167:801-807 [June 14] 1958) an article by Robert W. Wilkins, M.D. entitled "Precautions in Use of Antihypertensive Drugs, Including Chlorothiazide," in which the author mentions in the discussion of chlorothiazide, "It has no serious toxic effects, at least so far as is now known, although a few instances of skin rash have been noted among patients taking this drug."

# Epidemic Due to Microsporum Canis

**EDWARD H. FERGUSON, M.D., Monroe, Wis.**

Although tinea capitis and tinea circinata caused by Microsporum canis are fairly common diseases, they most often cause sporadic infections.[1,2] In the summer of 1957, a sudden small epidemic involving at least 12 persons occurred in a small town, and all cases could be traced to one kitten.

The entire family, both parents and three children, who owned the kitten were infected, as well as eight other persons in the immediate neighborhood. One child who lived several blocks away was a frequent visitor at the home where the kitten lived and also became infected. Of the 12, Two were adults; 2 were adolescents, and 8 were children from 2 to 8 years of age. All 12 developed typical lesions of tinea circinata with oval erthyematosquamous patches with involuting centers and "active borders." Only two children developed tinea capitis, and these cases were of the noninflammatory type. The kitten and both children showed hairs with typical green fluorescence under Wood's light. Hairs from all three were positive KOH, as were skin scrapings from the lesions of those without tinea capitis. All were examined initially in a two-week period, and M. canis was eventually cultured from all cases seen. It is of interest that one new pet could be responsible for such a sudden small-scale epidemic.

2425 Geary Blvd., San Francisco.

Submitted for publication April 28, 1958.

From the Department of Dermatology, The Monroe Clinic.

Present address: 2425 Geary Blvd., San Francisco.

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# Correspondence

## HAIR CASTS AND NITS

*To the Editor:*—I stopped this particular "epidemic of head lice" A. M. A. ARCH. DERMAT. [July] 1958) when I explained to the authorities that those who were examining the scalps of these school children were seeing hair casts instead of nits (Kligman, A. M.: Hair Casts, A. M. A. ARCH. DERMAT. 75:509 [April] 1957, and Brunner, M., and Facq, J. M.: A Pseudoparasite of Scalp Hair, ibid., p. 583) and making erroneous diagnoses of head lice without corroboration by microscopic examination. Fortunately for everyone concerned, the newspapers played down the fiasco, and, as far as I know, irate parents let the matter drop.

Now I read that the Portland, Ore., schools are apparently experiencing the same difficulties that the Los Angeles schools did. I am sure they are having hair cast trouble, too.

I have a premonition that a pandemic of scalp misdiagnoses will occur this autumn when school opens. I strongly urge you to alert the proper authorities. School nurses, particularly, should be taught the differential diagnosis of hair casts and nits. An alert now should obviate needless anguish and impaired professional reputations.

C. RUSSELL ANDERSON, M.D.
416 N. Bedford Dr.
Beverly Hills, Calif.

## KERATOACANTHOMA VERSUS SQUAMOUS-CELL CARCINOMA

*To the Editor:*—I was very interested in the recent article (A. M. A. ARCH. DERMAT. 77:390, 1958) "Keratoacanthoma Versus Squamous-Cell Carcinoma," by Drs. Moragas, Hamilton Montgomery, and McDonald. In a short paper on keratoacanthoma read at the Annual Meeting of the British Association of Dermatology in 1956 I made mention of one of the histological findings so clearly described by the above authors—namely the constant and well-marked inflammatory response occurring in the dermis close up to the base of all keratoacanthoma lesions. Considering this, and the extremely superficial placing of all these lesions, combined with the complete resolution of the lesions without treatment, I was emboldened to make a suggestion on etiology. I felt the major factor was an external one, in all probability a virus.

I wonder whether any of your readers, having viral investigation facilities at hand, have already gone into this. I would be very grateful indeed to hear of their findings. The difficulties of diagnosis may have hitherto prevented any large-scale viral investigations; however, we do know nowadays that the tumor is by no means a rarity in our clinics, and perhaps this line of investigation might well be considered, if indeed this has not already been done.

ALLAN BIGHAM, M.D.
6 Mornington Villas
Manningham Lane
Bradford 8, Yorkshire
England

## BCG VACCINE

*To the Editor:*—The recent report of the Ad Hoc Committee of the Surgeon General of the United States, after weighing the advantages and disadvantages of BCG vaccination, states: "It is believed, however, that the advantages of vaccination outweigh the disadvantages for tuberculin negative persons who are exposed to a definite risk of infection, especially if they cannot be retested frequently with tuberculin."

This Committee recommended BCG vaccination for those groups recommended by the American Trudeau Society, the American College of Chest Physicians, the American Medical Association, and the Medical Advisory Committee of Research Foundation.

The specific groups recommended for BCG vaccination by the American Trudeau Society are the following: (1) doctors, medical students, and nurses who are exposed to tuberculosis;

(2) all hospital and laboratory personnel whose work exposes them to contact with the bacillus of tuberculosis; (3) persons who are unavoidably exposed to infectious tuberculosis in the home; (4) patients and employees in mental hospitals, prisons, and other custodial institutions in which the incidence of tuberculosis is known to be high; (5) children and certain adults considered to have inferior resistance and living in communities in which the tuberculosis mortality rate is unusually high.

There have been numerous inquiries from all parts of the United States as to where BCG vaccine may be obtained. In order to assist those interested, the following information is offered: BCG vaccine may be obtained by any licensed physician in the United States and its territories by writing to the laboratories of Research Foundation and the University of Illinois, the only institutions licensed to produce and distribute BCG in this country. The address of Research Foundation is 70 W. Hubbard St., Chicago 10.

Sol Roy Rosenthal, M.D., Ph.D.
Medical Director, Research Foundation, and
Director, Institution for TB Research,
University of Illinois

# Obituaries

## Prof. DR. J. J. ZOON

Prof. Dr. J. J. Zoon died at the age of 55 years, on Jan. 28, 1958.

Professor Zoon received his medical education at Utrecht. He was an assistant (1927-1929) and then chef de clinique at the dermatological clinic of the State University of Utrecht. In 1946, he succeeded Prof. Dr. Th.M. van Leeuwen.

Professor Zoon was a robust personality who always went straight to the point, who never was deceived by outward appearances, and who disliked hollow phrases.

He was a good friend, as many Americans will remember; he made two visits to America, the first in 1947 (on the invitation of the Rockefeller Foundation)

PROF. DR. J. J. ZOON
1902-1958

and the second as a foreign guest of honor in 1955, when he delivered four speeches before the American Academy of Dermatology and Syphilology at Chicago.

Although he had been ill for a long time and even seriously ill for the last years, he never refrained from continuing with unabated zeal what he considered to be his duty.

Professor Zoon was a conscientious and critical worker. About 100 of his articles were published. The so-called balanitis plasmocellularis which he described in detail received the name of Zoon's disease. Although he was a dermatologist of the morphological period, he realized that the basic sciences such as physics and chemistry are necessary to further the knowledge and the treatment of skin diseases. He always had a great interest in the fight against syphilis and the social problems connected with it.

This excellent didactician considered the education of his students as his most important task, and he loved his personal contacts with them.

Professor Zoon was greatly appreciated as a dermatologist both at home and abroad, and in addition to his being a member of honor of the Dutch dermatological association he was a member of honor and a correspondent member of several foreign dermatological associations.

His indefatigable work led to the building for the State University of Utrecht of one of the most modern dermatological clinics in Western Europe. This will be equipped with a chemical and physical laboratory, where the investigation of light sensibility of the skin will form one of the most important lines of research. His preliminary experiments (Untersuchungen über die Empfindlichkeit der Haut für ultraviolette Strahlen bei Patienten mit Xeroderma pigmentosum, *Strahlentherapie,* 1938) showed that he had a great interest in this subject.

Professor Zoon was the "boss" for his collaborators and their friend. Nobody ever asked in vain for his advice and support. His death leaves a gap for his wife and children but also for his staff. We who are his disciples shall remember him gratefully for his friendship, the way in which he moulded us into dermatologists and indicated to us new lines to approach dermatological problems.

L. H. Jansen
Utrecht, Netherlands

## GEOFFREY RAKE, M.D.

### 1904-1958

Although he was not a dermatologist by formal training, Geoffrey Rake's research and scholarly efforts in this field wrought profound changes in the understanding and management of skin and venereal diseases. Of his more than 150 publications, only a few can be singled out here. Among the original contributions which he and his colleagues made are these: a simple method of testing drugs against tuberculosis which led to the discovery of isoniazid; the growth of lymphogranuloma venereum virus in the chick embryo yolk sac for the preparation of the now universal skin test and serologic test for this disease; the growth and elucidation of the Klebsiella bacterium which causes granuloma inguinale; the first portrayal of the herpes simplex virus with the electron microscope and the first demonstration with this instrument of the identity of the chickenpox and zoster virus. As one of the original members of the Syphilis Study Section and of the Virus and Rickettsial Study Section of the United States Public Health Service, he was one of the architects of the penicillin treatment of syphilis and of the recent vast growth in knowledge of viral and rickettsial diseases. When his friend, Howard Florey, brought from England the first cultures to prepare penicillin in the United States, they were entrusted to Rake, who then played a dominant role in the American scientific production miracle with this drug which has saved untold lives throughout the world.

This friendly, tireless man was born in England in 1904 and received his medical education at Guy's Hospital, London University, where he won the Gold Medal in medicine and other honors. In 1928, he came to Johns Hopkins University to work in pathology and later studied at the University of Heidelberg. In 1930, he moved to the Rockefeller Institute, where he worked in microbiology until 1936, followed by a year at the University of Toronto. In 1937, he joined the Squibb Institute for Medical Research and remained in various capacities with Squibb and the Olin Mathieson Corporation, finally becoming scientific director of the international division in 1956. During this period he simultaneously held the following positions: Research Professor of Microbiology in the University of Pennsylvania School of Medicine and School of Veterinary Medicine, Chairman of the Research and Grants Committee of the New York Cancer Committee, a director of the New York Women's League for Animals (E. P. Speyer Hospital), mayor of Milstone, N. J., where he resided, and many others. His membership in the Society for Investigative Dermatology, among a long list of societies of which he was an honored member or fellow, was a favorite of his.

A memorial service to this great scientist, scholar, and humanist, who died of a coronary occlusion on April 20, at the age of 53, was held by his friends at the Quaker Meeting House in Princeton, N. J. There were many to speak of his integrity, his modesty, and his great achievements, but there are multitudes everywhere who will forever benefit from his contributions to scientific medicine and dermatology. Our great loss is exceeded only by that of his loyal wife, Helen, and six children.

HARVEY BLANK, M.D.

## LORETTA JOY CUMMINS, M.D.

### 1883-1958

Dr. Loretta Joy Cummins died in Boston on Feb. 25, 1958, at the age of 75, after prolonged hospitalization following an accident.

Dr. Cummins was born in Chelsea, Mass., and received her elementary and high school education there. She graduated from Tufts Medical School in 1903 with the degree of M.D.

She interned at Memorial Hospital, Worcester, and took postgraduate work in dermatology at Vanderbilt, working under Dr. MacKee and Dr. Rosen. She worked for a considerable time at the Boston Dispensary with Drs. Lane and Blaisdell. She was the first woman to be appointed to the staff of the Massachusetts General Hospital when, in 1916, she was appointed Assistant Dermatologist, and in 1928 she was appointed Dermatologist. In 1940 she was placed on the Consulting Staff, and later on the Honorary Staff.

Dr. Cummins was the first woman to be President of the New England Dermatological Society, 1922-1923. She was President of the dermatological section of the Massachusetts Medical Society, and Vice-President of the Boston Dermatological Club. She held membership in the American Medical Association, Massachusetts Medical Society, New England Dermatological Society, Boston Dermatological Club, and American Academy of Dermatology and Syphilology and was certified by the American Board of Dermatology and Syphilology, as well as other organizations outside the medical field.

It is difficult to enumerate her attributes. She was a keen clinician, with continued interest in her chosen field. She was an excellent teacher, and, though without official title at Harvard Medical School, she did a great deal of unofficial teaching of the postgraduate students.

One of the rare vivacious persons who had a smile and cheery greeting for everyone, beloved by friends and patients alike, it was her earnest desire to be of help to others.

A most gracious and charming lady has passed from our midst, but, in spite of an incapacitating illness, with her chin up.

Austin Cheever, M.D.
Ethel Rockwood, M.D.

# The New, Newer, and Newest

With the end of summer, we should all become "meeting-conscious" again and begin thinking about the A. M. A. meeting next June. If you have material that merits a report at that meeting, you should communicate with the section secretary by December 1, because the officers meet to organize the program in Chicago during academy week.

Harry Arnold, of Honolulu, has been honored with a Corresponding Membership in the Venezuelan Dermatological Association.

Marc Caro has resigned his position of Professor and Head of the Department of Dermatology, University of Illinois College of Medicine.

Despite all our efforts, errors continue to appear on this page. In the July ARCHIVES we "goofed" the punctuation and a comma separated Falco from Otto Braun-Falco of Germany, one of the participants in the psoriasis conference sponsored by the New York Academy of Sciences last May. Now we learn that Carl Nelson was Chairman for one session, not the whole meeting as we had announced. The entire affair—gathering the participants, editing and translating papers, keeping everybody happy, etc.—was the work of the General Chairman, Peter Flesch—the well-named dermatologist!

Several states, apparently, will soon repeal laws requiring compulsory premarital blood tests for the simple reason that the law has failed in its primary aim—to uncover contagious syphilis. The monies spent in enforcing the law could better be used in areas of more practical and scientific methods of venereal disease detection.

Aug. 15-Sept. 15 is National Allergy Month by proclamation of the Allergy Foundation of America, which appears to be a professionally managed publicity arm for allergists, and actually there is legislation pending in Congress designed to authorize the President to issue a proclamation designating a National Allergy Month each year.

Have you noticed the euphonious term "Lousicide" that appears in a drug advertisement?

The new officers of the Washington, D. C., Dermatological Society are Raymond Osbourn, Chairman; Peter N. Horvath, Vice-Chairman, and June C. Shafer, Secretary.

The New England Dermatological Society, which meets four times a year and usually in Boston, has elected Joseph Goodman, President; Paul J. Catinella, Vice-President, and William R. Hill, Secretary.

The Noah Worcester Dermatological Society, born last April, "out of Cincinnati," has already set a date for its next meeting in Miami Beach, April 7-11, such lucky members could only portend a successful session. Those who are interested may learn details at a dinner meeting being arranged for Dec. 8, in Chicago, during academy week.

Dr. David W. Kersting has been appointed Professor and Chairman of the Department of Dermatology at Marquette University School of Medicine, succeeding Dr. Harry R. Foerster who becomes a Clinical Professor Emeritus. Dr. Kersting is the director of graduate training in dermatology at the Veterans' Administration Hospital at Wood and at Marquette, and he is Chief of the Dermatology and Syphilology sections at Wood.

Now that hydrocortisone for compounding prescriptions is available, William B. Swarts, of Greenwich, Conn., urges dermatologists to behave more like dermatologists by prescribing special compounds for particular situations.

Succinct and Sagacious: "In general, it may be suggested that in the balance between host defenses and microbial attack, antimicrobial agents usually aid the host, whereas corticosteroids often aid the parasite." (Kass, E. H.: *A. M. A. Arch. Int. Med.* 102:1 [July] 1958.)

"In contact dermatitis, the causative agent is everything . . . in atopic dermatitis, the host. . . ." (R. L. Mayer, "Transactions of Collegium Internationale Allergicum," 1958.)

H. R.

# Society Transactions

## CHICAGO DERMATOLOGICAL SOCIETY

**Adolph Rostenberg Jr., President**
**Samuel M. Bluefarb, Secretary**
**Jan. 15, 1958**

**Sickle Cell Anemia with Leg Ulcer.** Presented by Dr. Samuel Bluefarb, Dr. Silas Wallk, and (by invitation) Dr. Martin L. Gecht.

This 21-year-old Negro woman developed an ulcer on the medial surface of the right ankle three years ago. This lesion has never healed.

One year ago the patient was admitted to Cook County Hospital complaining of chills and fever. These episodes have been repeated several times during the past year. The diagnosis of sickle-cell anemia was made at that time.

She states that she has had "yellow eyes" as long as she can remember.

Laboratory Findings: Sickle-cell preparation, positive. Hemoglobin electrophoresis, homozygous S.

### Discussion

Dr. Francis W. Lynch, St. Paul, Minn.: It is noteworthy that it has been found that patients with sicklemia or sickle-cell anemia are subject to risk of splenic infarction when at high altitudes in flying. Understandably, the laboratory data available as yet are not adequate for certainty of diagnosis in this case. A hurried inquiry suggests that she has had since childhood recurrent chills, fever, and possible icterus, suggesting congenital hemolytic icterus, which can, of course, lead to similar chronic ulceration of the leg.

Dr. Samuel M. Bluefarb: I should like to call attention to another report on this condition, which appeared in the *British Medical Journal*. The investigators found that a lowered or reduced amount of hemoglobin was responsible for the sickling of the cells in these patients. It was found that the addition of Diamox (acetazolamide) to this blood, in a test tube, resulted in inhibition of sickling. In one patient they were successful in increasing the hemoglobin level with the administration of Diamox.

**Linear Scleroderma.** Presented by Dr. Samuel Bluefarb, Dr. Silas Wallk, and (by invitation) Dr. Martin L. Gecht.

This 14-year-old white girl was first presented to this Society in February, 1956. Lesions were first noticed on the upper left arm in 1951, when the patient was 8 years of age. The process became more extensive, gradually involving large parts of the left arm, the back of the neck and trunk, anteriorly and posteriorly. There were many sclerotic, white, shiny plaques, some of which developed fissures and scaling. During the severe stage, she had some limitation of motion of the left shoulder and left thumb. These areas began to heal subsequent to the administration of chloroquine, 375 mg. daily, which was given for two years. The mother states the improvement was dramatic from the very beginning of therapy. As the lesions healed, they left a depressed scar, as well as hyperpigmentation. Today most of these depressed areas are level with the adjacent normal skin, but the hyperpigmentation has remained. Some areas have healed without depression or hyperpigmentation. There have been no intercurrent illnesses other than upper respiratory infections. During one of these latter episodes, she received a sulfonamide drug. Within 24 hours the lesions became erythematous, but this disappeared when the sulfonamide drug was discontinued. She has not taken any chloroquine for two months, and there has been no noticeable change in her condition.

### Discussion

Dr. Leon Goldman, Cincinnati: In some cases of linear scleroderma in children we have been faced with the possibility of the development of spontaneous amputation and necrosis. In connection with scleroderma of the extremities which is still spreading and which is not responding in due time, we have had consultations with plastic and orthopedic surgeons. The results have been interesting. Experienced plastic surgeons have been able to put full-thickness grafts in areas that are almost completely bloodless. Such grafts can prevent contracture and make an active child out of a cripple. We have seen several grafts which did not become sclerodermatous. For local areas, hydrocortisone, injected underneath the skin, does give improvement. We still use nicotinic

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acid esters or nicotinic acid itself in ointment form as massage therapy.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: Studies made by Dr. Christensen when at the Clinic, in a review of linear scleroderma in children, revealed that about 40% had hemiatrophy and a very small percentage of these had brain lesions. Orthopedic corrections for defects of the feet are necessary in cases of linear scleroderma. I believe linear scleroderma and morphea are essentially similar processes. In morphea one has "spots" and does not have deformities.

DR. ADOLPH ROSTENBERG JR.: I think it is an error to call scleroderma and morphea the same thing, as clinically morphea behaves differently. Whether linear scleroderma and morphea are the same is questionable. How often morphea is associated with linear scleroderma is another matter. In this event, it could be called linear scleroderma plus morphea, but I think it would be an error to give up the name morphea.

DR. STURE A. M. JOHNSON, Madison, Wis.: Because we recently have had two papers published on scleroderma in the *Journal of Investigative Dermatology* (*29*:273 and 289, 1957), I rise to discuss this case. It appears at present that persons with various diseases vary in their metabolism of tryptophan. The differences after a tryptophan load in urinary quantities of the various products of tryptophan metabolism may be so characteristic that help in making a diagnosis might be forthcoming when it cannot be made clinically. For instance, such information might help to differentiate acrosclerosis and sclerodactylia. After chelation with edathamil sodium, we have noted changes in the products of tryptophan metabolism in patients with acrosclerosis and other conditions. Clinically, we have seen the skin become looser, the joints less stiff, the ulcers of the fingers less noticeable, the intolerance to cold less marked, and the facies less mask-like. In patients with diffuse scleroderma, who have been almost moribund at the time of starting treatment with edathamil sodium, we have seen early favorable changes, which unfortunately were not permanent.

DR. LOUIS RUBIN, Rockford, Ill.: I should like to ask a couple of questions. It seems to me that we see linear scleroderma uniformly starting in the very young. We often see linear scleroderma and morphea together in the same patient, but it seems that morphea does not as uniformly start at as early an age as linear scleroderma.

I should like to ask the presenters a question. I have information from the mother that she thinks that the linear scleroderma lesions improved with the treatment but that the lesions of morphea did not respond. I wonder if this indicates a basic difference in the conditions, or if the story is true.

**Papulosquamous Disease: Psoriasis; Lichen Planus?** Presented by DR. THEODORE CORNBLEET, DR. SIDNEY BARSKY, and (by invitation) DR. HASSAN YAZDI.

This 35-year-old Negro man stated that he developed erythematous, papular, and scanty eruption on the forearms and legs about six months ago. New lesions gradually involved the trunk and extremities. He complains of severe itching.

A biopsy specimen is presented.

### Discussion

DR. HERMANN PINKUS, Monroe, Mich.: We have a special name for this in Detroit. We call it Keim's disease for one of our senior members. Dr. Harther L. Keim likes to think of these cases as a metamorphic syndrome. They usually start as ordinary pityriasis rosea but instead of clearing up they develop either into psoriasis or lichen planus. I always suspected that these cases from the beginning were lichen planus or psoriasis but have the clinical appearance of pityriasis rosea during the first few weeks. In some biopsy specimens we took from cases when they first came to the clinic, the histologic picture usually was diagnostic of lichen planus or psoriasis. In today's case the biopsy specimen did not show any changes of lichen planus. It seemed to show some features of psoriasis, such as acanthosis and some wide-open capillaries in the long papillae. I feel that eventually this patient will have a typical case of psoriasis.

DR. ADOLPH ROSTENBERG JR.: The members will recall a man presented by Dr. E. A. Oliver and me who exhibited both psoriasis and lichen planus.

There are interesting case reports on this combination. Fordyce had a patient for whom he would make a diagnosis of lichen planus on one visit and of psoriasis on another. Brocq spoke of all these conditions as cutaneous reactions that could convert into one another because they are not truly independent diseases. Dr. Moses Scholtz in 1936 wrote an interesting article in the *Archives* in which he considered the dynamic aspects of morphology.

DR. THEODORE CORNBLEET: We were going to apologize for showing a mere papulosquamous eruption at an Annual Meeting. The appearance of the lesions was so very different from time to time, the histological changes so indeterminate, and altogether this patient has been such a problem to us that we decided to show him. It has been our experience, too, that when these papulosquamous problems in differential diagnosis appear on the face, and especially on the lips, they often turn out in the end to be lichen planus.

**Senile Dermatitis Herpetiformis.** Presented by Dr. James Webster,† Dr. Stanley Huff, and (by invitation) Dr. Hassan Yazdi.

This 71-year-old Negro man stated that he was quite well until September, 1957, except for two abscesses on the buttocks which were treated for about a month and a half previously. At that time he developed an erythematous and bullous eruption on the back of the neck, which gradually spread to involve face, scalp, trunk, and extremities. No bullae appeared on the mucous membrane. The lesions are pruritic and grouped on the trunk and extremities.

Laboratory Findings: Hemoglobin 80%; white blood cells 4750; serology negative. Blood chemistry studies: NPN 43; sugar 130; total protein 5.2 (albumin 3, globulin 2.2); potassium 6.1; thymol turbidity 1.2; cephalin flocculation 0; γ-globulin 0.88.

A biopsy specimen is presented.

**Pemphigus Vulgaris.** Presented by Dr. Otto C. Stegmaier.

A woman, aged 61, was first seen in the office on Nov. 25, 1957. The patient has had extensive erosions of the alveolar mucosa, both upper and lower, since September, 1956. The lesions begin with vesicles near the teeth. Within a few hours the surface disappears leaving a bright ruby-red erosive surface. Originally the erosions were on the lingual surface near the teeth, and lately they have been on both sides of the alveolar ridge. There have been no lesions elsewhere. Treatment by her family physician has consisted of hydrocortisone locally and Meticortin orally (dosage not known) for about 30 days. She also had Stilbestrol, vitamins, and Achromycin prescribed by her family doctor without any benefit. She has been on Carbarsone, 0.4 gm. three times a day for four days of each week for the past five weeks without any benefit. On Jan. 6, she was placed on Fowler's solution.

Biopsy specimen and microscopic slide are presented.

### Discussion

Dr. Henry E. Michelson, Minneapolis: I presume one might remark that there is not much in a name, providing one knows precisely what the name implies. I think there is a great difference when we are trying to differentiate between diseases as serious as pemphigus and one that is troublesome but not so serious, as dermatitis herpetiformis. A number of years ago, before the microscopic diagnosis was so emphasized, I believe all of us would have called this case one of pemphigus. Since then, the name pemphigoid or senile dermatitis herpetiformis has been used a great deal. For my own part, I think the diagnosis should still be pemphigus, even though it is milder than some of the other forms. It is a disease that is capable of killing and responds only to the steroids. Certainly no other cases of dermatitis herpetiformis respond to the steroids. I believe that the line between dermatitis herpetiformis and pemphigus is a sharp one and that they are two entirely different entities.

The other patient presented as pemphigus of the mucous membrane is, of course, difficult to diagnose. I have not seen pemphigus of the mucous membrane confined to the gingiva. A while ago I took part in a symposium with a group of stomatologists and dentists, and they showed some cases similar to the one shown today which they called herpetic gingivitis. That might be considered here.

Dr. Allan Lorincz: I would like to suggest benign mucous membrane pemphigus or ocular pemphigus as a possible diagnosis in Dr. Stegmaier's patient.

Dr. Julius E. Ginsberg: The larger bulla was loaded with eosinophils. Many people would call these pressure bullae. Can eosinophils occur in this abundance in pemphigus?

Dr. Clark W. Finnerud: Years ago, Dr. Ormsby presented a case of presumably cured pemphigus. This patient had been previously presented when the eruption was severe, and all agreed with the diagnosis of classical pemphigus vulgaris. He had remained entirely free of symptoms for more than a year at the time he was last demonstrated. Shortly after that, however, he had another attack, which terminated fatally. One of the interesting things about that patient was that in the sections and in the blood the cells were practically entirely eosinophils. All the sections showed more eosinophils in the bullae and in the infiltrate than we had ever seen in dermatitis herpetiformis.

Dr. Stephen Rothman: Was it pemphigus, if it was cured?

Dr. Clark W. Finnerud: Everybody agreed it was pemphigus, but it eventually proved not to be cured.

Dr. Isadore Fisher, Minneapolis: In the cases at the University of Minnesota Hospitals that we reviewed, there were a number of patients who had large numbers of eosinophils in the peripheral blood also. In some cases the eosinophil count ranged from 40% to 60%. These were patients who exhibited the clinical picture with all the signs and symptoms of pemphigus vulgaris.

Dr. Stanley Huff: These cases always present a difficult problem clinically and histologically. I am sure the presenting diagnosis often is influenced by geographic location. For example, the

† Dr. Webster died Feb. 28, 1958.

same case might be presented in Minnesota as pemphigus, in New York as dermatitis herpetiformis, in England as pemphigoid, and here at Cook County Hospital as bullous erythema multiforme.

One other thing to be considered in this patient is some form of internal malignancy. Recently I have seen a patient with Hodgkin's disease with cutaneous lesions indistinguishable from dermatitis herpetiformis.

**Dermatomyositis.** Presented by DR. THEODORE CORNBLEET, DR. SIDNEY BARSKY, and (by invitation) DR. MARTIN L. GECHT.

This 40-year-old white woman was admitted to the hospital on Jan. 11, 1958, complaining of weakness of her arms and legs of six months' duration. She has been unable to dress, comb her hair, or ambulate without assistance. During this period she noted that her arms, neck, chest, and abdomen have become darker. Her face became slightly edematous and markedly erythematous. The abdomen has become progressively distended. She has suffered profuse night sweats and has lost about 30 lb. On admission she appeared to be lethargic. The temperature was 101 F, and a nontender mass about 6×6 cm. was felt within the lower part of the abdominal wall. No abnormalities were detected in the genitourinary tract or in the rectum.

Laboratory Findings: Hemoglobin 93%; white blood cells 5650 with 65 polymorphonuclears, 28 lymphocytes, 7 monocytes. Urinalysis: No abnormalities. L. E. preparation, negative. Erythrocyte sedimentation rate 42 mm. in an hour. Blood chemistries: Total protein 7.9 mg/100 cc.; γ-globulin 2.30 gm/100 cc.; icterus index 12; thymol turbidity 8.8 units; cephalin flocculation 2+. Serology (Kahn) negative.

Chest and upper gastrointestinal tract x-rays normal. Transaminase, 7 units (normal to 30). Creatinine clearance not completed.

Biopsy study of skin and muscle not completed.

**Dermatomyositis?** Presented by DR. FREDERICK D. MALKINSON, DR. LOUIS RUBIN, and (by invitation) DR. E. MANFRED BLONER.

A 48-year-old electronics assembly foreman was first seen in our Dermatology Clinic on Dec. 30, 1957, with the complaint of fatigability, shortness of breath, and a skin eruption. In January, 1957, he noted the onset of redness and scaling on h. hands, knees, and elbows. That condition was treated with topical applications and four x-ray treatments at weekly intervals to the hands, without improvement. In April, 1957, the patient first noticed easy fatigability, shortness of breath on exertion, and pain in the calf muscles when walking, forcing him to give up working around the house. By this time, there was a definite loss of appetite and a weight loss of about 20 lb. The patient also complained of redness around the eyes and on the ears, as well as a low-grade fever (up to 100 F in the afternoon) and chills. In June, 1957, he was hospitalized elsewhere for three days, where the diagnosis of subacute lupus erythematosus was made, and he was discharged on 10-15 mg. of Meticorten daily, as well as antimalarials. On this regimen he soon regained his appetite and weight, being able to return to full-time work by Sept. 1, 1957. In December, 1957, he noted the onset of abdominal tenderness when bending forward or when yawning. The erythema and scaling extended by that time to the scalp, midface, and anterior chest. Also, dyspnea was apparent even on mild exertion. An asymptomatic nodule in the thyroid, noted on admission, had allegedly been present for the past four years.

On admission to the University of Chicago Hospital on Jan. 5, 1958, the positive physical findings were as follows: A nodule in the right lobe of the thyroid was found to be firm, mobile, and nontender (will shortly be excised). Lungs: rales in both lower lung fields at height of inspiration.

Skin Findings: Patchy erythema of the scalp. Red, dusky erythema of the eyelids, cheeks, nose, and chin. Edema of the upper eyelids. There was erythema and minimal scaling of the mid anterior chest, extensor elbows, and knees. Dusky erythema was present on the palmar aspects of the hands, as well as on the knuckles, extensor aspects of the finger joints, and periungually.

Laboratory Findings: Hemoglobin 14.8 gm.; red blood cells 4,380,000; white blood cells 6100, with normal differential count. Kahn nonreactive. BMR −2%. Total plasma protein 6.9 gm. % (albumin 3.2 gm. %, globulin 3.7 gm. %). Serum alkaline phosphatase 2.2 units (normal). L. E.-cell test negative. Cholesterols: total 260 mg. %, esterified 165 mg. %. Creatinine in 24-hour urine specimens: 0.15 gm/1000 cc. of urine. Creatinine 1.52 gm/1000 cc. of urine. Sputum smears were negative for acid-fast bacilli. ECG within normal limits.

The chest x-ray showed an area of probable pneumonia in the left costophrenic angle. Chest fluoroscopy revealed poor mobility of the diaphragms, bilaterally.

Pulmonary function tests revealed a moderately severe restriction of the vital capacity but no arterial oxygen desaturation. There was a restriction of the pulmonary diffusing surface, or an "alveolar capillary block," of slight degree. These findings are compatible with pulmonary fibrosis.

Complete gastrointestinal series showed no abnormality. There was normal peristaltic activity in the esophagus. Proctoscopy revealed no abnormality.

Section of a muscle biopsy specimen from the left deltoid shows normal skeletal muscle.

Skin section from the presternal area shows acanthosis, focal parakeratosis, spongiosis, and a mild chronic inflammatory infiltrate in the corium. Skin section from the knuckle shows perivascular edema and inflammatory-cell infiltrate. Skin section from the facial eruption shows parakeratosis and mild inflammatory changes. All sections are presented.

Skin tests were performed with toxoplasmin, Trichinella antigen, O. T., coccidioidin, and histoplasmin; all were negative after 48 hours.

**Case for Diagnosis.** Presented by DR. JULIUS E. GINSBERG.

A 47-year-old white woman was first seen on Jan. 13, 1958, complaining of generalized pink-to-dusky-red slightly raised streaks and patches on the skin and of scaling of the scalp. She also complained of itching of the scalp and ears. The first spots were noted about the nail folds four years ago and within the next year about the extensor surfaces of the arms and the anterior superior exposed chest area. Areas on the face appeared within the past eight months. The scalp has been erythematous about two years. She has felt well and continued ordinary housework up to present time. There is no cutaneous or muscular tenderness or pain.

Internal medications from Oct. 20, 1956, to present include phenobarbital, Seconal, Aralen, Plaquenil, Miltown, Tuinal, Aquasol A (vitamin A), vitamin $B_{12}$, and Chlor-Trimeton.

Laboratory Findings (Mayo Clinic, Report of Dr. Louis A. Brunsting): Chest x-ray O. K. (Ghon complex). Complete blood cell count essentially normal. Kline and L. E. clot test negative. Sedimentation rate 22 mm. in an hour (Westergren). Serum G-O transaminase normal. Serum proteins 7.75 gm., of which 4.95 gm. was albumin. The pattern of electrophoresis was normal.

Biopsy of skin lesion, dorsum of the left thumb: No clear-cut evidence of L. E.

## Discussion

DR. LOUIS BRUNSTING, Rochester, Minn.: The cases presented as dermatomyositis show the extreme range of the symptomatology of this disease. In some, muscular weakness in the form of polymyositis, even resembling myasthenia gravis, may be present for a matter of months or years before the eruption appears, or the eruption may not appear at all. In others, muscular weakness is minimal, and the skin signs predominate, occasionally assuming the pattern of a universal state. Mottling or poikiloderma may be prominent over the exposed surfaces and may be difficult to differentiate from chronic lupus erythematosus. In the diagnosis of dermatomyositis, the muscle biopsy is not the last word. In contrast to lupus erythematosus, patients with dermatomyositis manifest a profound weakness rather than fatigue. There is usually very little fever except in the acute phase; the sedimentation rate is not particularly elevated; the electromyogram may show significant change in motor potentials, and visceral complications are minimal except that occult malignancy may be present. In dermatomyositis, a true index of the activity of the disease may be formed from the level of the serum glutamic oxalacetic transaminase.

DR. STURE A. M. JOHNSON, Madison, Wis.: Was porphyria suspected in Dr. Ginsberg's case?

DR. JULIUS E. GINSBERG: I did not study the urine for porphyria. I suspected there was a sensitization of some sort. Perhaps that was done at the Mayo Clinic.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: I do not think so.

DR. THEODORE CORNBLEET: The association of malignant change in the ovary or other part and dermatomyositis has been reported. The gynecologist found no pelvic abnormalities in our patient. We have not found transaminase determinations too useful; apparently the muscles must be in very active deterioration to produce significantly elevated values. The internists thought our patient might have pellagra, but I think dermatomyositis is a reasonable diagnosis.

DR. FREDERICK D. MALKINSON: In reply to Dr. Brunsting, this patient has had both a gastrointestinal series and barium enema, and no evidence of gastrointestinal tract tumor has been found. We, too, are interested in the problem of the thyroid tumor here, especially because of the known association of carcinoma with dermatomyositis. The surgeons have seen the patient, but, because of skin involvement nearby, they prefer to postpone surgery for now and reexamine him in a month. It is interesting, however, that endocrine gland tumors have been reported only rarely in association with dermatomyositis, although chromophobe adenoma of the pituitary has been found to accompany this disease.

The most interesting feature of this patient, perhaps, is the pulmonary involvement, which accounts for his disturbing fatigue and his dyspnea, even at rest. His vital capacity is markedly diminished, and this, together with slight capillary alveolar block found on pulmonary-function studies, suggests a diffuse interstitial fibrosis. In addition, the movements of the diaphragm are also markedly impaired. While diffuse fibrotic pulmonary changes have been described previously in dermatomyositis, they are rarely encountered, and it is most unusual that they should account for the main symptomatology of the disease. The possibility remains, however, that primary involvement of the diaphragm and intercostal muscles accounts for the patient's pulmonary complaints.

**Nevus Unius Lateris from Axilla to Leg.** Presented by DR. DAVID OMENS, and (by invitation) by DR. HAROLD OMENS and DR. J. LATONI.

**Bathing Trunk Nevus with Neurofibromatosis.** Presented by DR. DAVID OMENS, and (by invitation) by DR. HAROLD OMENS and DR. MARTIN L. GECHT.

**Piebaldism.** Presented by DR. SAMUEL BLUEFARB, DR. SILAS WALLK, and (by invitation) DR. HASSAN YAZDI.

A 9-year-old Negro girl was born with large depigmented areas on the legs and a small depigmented area in the midline of the forehead with a white forelock. One year later she developed a number of pigmented spots on the white areas of the leg which gradually increased in size and in some instances became confluent.

Two of four siblings had similar depigmented patches at birth. One, 7 years of age, has a depigmented spot on the forehead; another, 4 years old, has depigmented areas on the lower extremities and a small spot on the forehead. The mother was born with a white forelock.

### Discussion on the Preceding Three Cases

DR. HERMANN PINKUS, Detroit: I would like to ask a question about the case presented as nevus unius lateris. It is unusual to have unilateral nevi in that diffuse distribution from the neck to the leg except in cases of ichthyosis hystrix. I wonder if this boy had Darier's disease, which can occur in this form. I think it would be well to take a biopsy specimen and find out what the histopathologic picture is.

Dr. Bluefarb's group of cases presented a very unusual feature. The mother stated that the areas of depigmentation are getting smaller and considerable areas have filled in. This is not what I would expect in a true case of piebaldism. It reminded me of what one sees sometimes in animal skin, where spotty epidermal pigmentation may occur quite independent of the color pattern of the hair. In the skin of a wirehaired terrier which I observed for several years, the dark areas of the skin increased with age and became almost confluent. This has been called infectious spread of melanin pigmentation. I have not been aware of this happening in human partial albinism and wonder if any of the other members is familiar with this phenomenon.

**Zosteriform Lichen Nitidus with Depigmentation.** Presented by DR. IRENE NEUHAUSER, DR. FREDERICK J. SZYMANSKI, and (by invitation) DR. ROLAND S. MEDANSKY.

**Lichen Nitidus.** Presented by DR. STEPHEN ROTHMAN and (by invitation) DR. BRIAN POTTER.

### Discussion on Preceding Two Cases

DR. HERMANN PINKUS, Detroit: Actually, there is nothing new or fashionable to report about lichen nitidus. No effective therapy has been proposed. No one has yet found any systemic connection; in this isolated corner there has been no "fertilization of general medicine by dermatological conceptions," as Dr. Ingram put it so nicely in a recent article (A. M. A. ARCH DERMAT. 77:79 [Jan.] 1958). In Dr. Rothman's case there was sudden onset, and the eruption is unusually widespread. In spite of this, the closely set papules do not become confluent, as one might expect if lichen nitidus really were just a variant of lichen planus. In the little Negro boy, the combination with depigmentation in a linear arrangement is interesting, but I can not see any reasonable connection between the vitiligo-like loss of pigment and the papular eruption, which started in the same region but now has spread to other areas of the back and has lost its "zosteriform" distribution.

**Leprosy—Lepromatous Type.** Presented by DR. S. M. BLUEFARB, and (by invitation) DR. J. HASEGAWA and DR. F. DUNLAP.

**Leprosy—Type (?).** Presented by DR. ROGER W. PEARSON and DR. DOROTHY B. WINDHORST (by invitation).

### Discussion on Preceding Two Cases

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I believe that the first case of lepromatous leprosy is clear-cut. The classification of leprosy in Ormsby and Montgomery is completely out of date, and it is difficult to keep up with the variations and classifications suggested at the different congresses on leprosy. I prefer the classification of Dr. Cochrane, who divides leprosy into the lepromatous, dimorphous, and tuberculoid forms. The Lucia phenomenon, which is endemic in Mexico and is part of lepromatous leprosy, reveals necrotizing vasculitis.

I believe the second case would fit in with the dimorphous type. The latter type may become lepromatous under certain conditions, including following too intensive treatment.

DR. IRENE NEUHAUSER: Leprosy is a very protean disease and may present a number of clinical pictures. From the standpoint of prognosis and therapy, it is important to classify each case of leprosy. At the present time two types of leprosy are recognized, the tuberculoid and the lepromatous types, and two less stable groups, the indeterminate and the borderline or diamorphous.

The patient presented by Dr. Bluefarb has the findings of a typical lepromatous leprosy. He has sharply defined, firm, smooth, nodular lesions;

alopecia of the outer portion of the eyebrows, and infiltrations in the ear lobes.

I think the second case is an early lepromatous leprosy. The histopathological section does not show both tuberculoid and lepromatous structures, which I believe is one of the characteristics of this group. It is unfortunate that Lepromin is so difficult to obtain, but I think more investigative work should be done on this patient. I noticed a number of globi in the histopathological sections, and I believe these are characteristic of the more malignant types.

DR. MONTGOMERY: I agree with you.

DR. NEUHAUSER: Globi are acid-fast spheroid bodies which are found in phagocytic cells and are thought to be degenerated phagocytized bacilli.

DR. SIDNEY J. KAPLAN, Waukegan, Ill. (by invitation): I saw this man (Dr. Bluefarb's case) years ago in a lepromatous crisis. The lesions at that time consisted of bluish-red macules on the lower abdomen, which on scrapings showed numerous organisms. As far as the origin of the disease in this man, he had years of contact with his father who served in the Philippines before World War I.

DR. J. HASEGAWA (by invitation): We went over this man's family history fairly thoroughly but did not elicit the history that his father had served in the Philippines. This man has been under observation since 1943.

**Rubber Girdle Area Depigmentation.** Presented by DR. THEODORE CORNBLEET, DR. SIDNEY BARSKY, and (by invitation) DR. J. LATONI.

**Arsenical Keratoses with "Dew Drop" Depigmentation.** Presented by DR. DAVID OMENS, with DR. HAROLD OMENS and DR. J. LATONI (by invitation.)

**Ophiasis.** Presented by DR. THEODORE CORNBLEET, DR. SIDNEY BARSKY, and (by invitation) DR. MARTIN L. GECHT.

**Secondary Syphilis.** Presented by DR. JAMES WEBSTER, DR. STANLEY HUFF, and (by invitation) DR. J. LATONI.

**Widespread Discoid Lupus Erythematosus.** Presented by DR. SAMUEL BLUEFARB, DR. SILAS WALLK, and (by invitation) DR. HASSAN YAZDI.

**Lymphoma.** Presented by DR. JOHN B. HAEBERLIN JR., DR. FREDERICK J. SZYMANSKI, and (by invitation) DR. GEORGE FLEMING.

**Rosacea with Acne and Edema.** Presented by DR. S. M. BLUEFARB, and (by invitation) DR. F. LEVIT and DR. J. HASEGAWA.

**Pityriasis Lichenoides et Varioliformis Chronica; Psoriasis?** Presented by DR. ALFRED B. FALK and DR. STEFAN BIELINSKI.

**Bowen's Disease.** Presented by DR. BRUCE BAIRSTOW.

## DETROIT DERMATOLOGICAL SOCIETY

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**Jan. 8, 1958**

**Alopecia Mucinosa.** Presented by DR. HERSCHEL ZACKHEIM.

A white boy aged 12, of average build, presented a fine follicular papular eruption on the back of the neck, both popliteal spaces, shaft of the penis, coccyx, and right sacral areas. The papules were flesh-colored, discrete, somewhat shiny, and about 1 mm. in diameter. On the back of the neck they were closely set together and covered most of the skin surface. In the popliteal areas they were spaced farther apart and were more numerous in the left space. The patches over the coccyx and sacral areas were less well defined. Both elbows were dry and rough.

The patient was first seen on April 5, 1957, because of the eruption on the back of the neck which had been present for about three or four months and a small patch of scaling alopecia on the left temporal scalp of one or two months' duration. Examination of the scalp lesion revealed some deformed and broken off hairs. Wood's light examination showed no fluorescence, and cultures of hairs were negative for fungi. In May he presented a new similar lesion of scaly alopecia in the right parietal area, about 3 cm. in diameter. Again Wood's light examination, culture, and direct examination of the hairs of fungi were negative. In late May and early June patches of follicular papules were noted in the above-described areas and on the right inner knee. The left temporal scalp lesion showed complete regrowth of hair in June, and the right parietal areas showed complete regrowth in July. All lesions were asymptomatic throughout.

Laboratory examinations revealed Hb. 15.0 gm., WBC 6700. Cholesterol, total lipids, total proteins, albumin, globulin, dextrose, and bilirubin were within normal limits.

Findings on biopsies of the neck, parietal scalp, and left popliteal regions showed essentially the same pathology, i. e., edema and a mucinous

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degeneration of the hair follicle, especially of the outer root sheath and sebaceous glands. Biopsy from the neck lesion: "The sections show no alterations of the epidermis and only minor perivascular infiltrates in the corium. The pathologic changes are associated with hair follicles and consist in the transformation of the sebaceous gland and the outer root sheath into mucin containing cysts and accumulations of mucin between the edematous cells of these parts. The hairs seem to be lacking in the affected follicles. There is moderate inflammatory infiltrate in the surroundings. Conclusions: Root sheath mucinosis" (H. Pinkus).

Treatment: Vitamin A, 50,000 units, was given daily for about three weeks in April and May, without effect. Ichthyol, 3% in zinc oxide ointment, and a 5% tar paste were without effect on the neck lesions. The papular patch on the right inner knee showed almost complete involution after four weekly doses of 75 r at 90 kv. None of the other areas were treated.

### Discussion

Dr. Hermann Pinkus, Monroe: I feel like a father who does not know what is going to become of his son. The first five cases on which the description of alopecia mucinosa was based were fairly similar clinically. Ever since publication of the article, cases of very different character have turned up. I am now aware of 10 recent American cases, including Dr. Zackheim's case.

Dr. E. B. Helwig told me that he located eight other cases in the files of the Armed Forces Institute of Pathology. He is apparently willing to agree that this is a pathologic entity. At the International Congress in Stockholm last summer, where I presented the histochemical findings of my cases, Dr. O. Braun-Falco (Mainz, Germany) discussed the paper and meanwhile published his findings in two cases that fit the clinical picture of alopecia mucinosa and in two other cases with similar histologic findings but in which the patients are suffering from systemic retriculosis or lymphoma. In addition, Dr. Szodoray, from Budapest, informed me he had published a similar case in 1939 (Lehner E., and Szodoray, L.: *Dermat. Wchnschr.* 108:679-685). This Hungarian case was of a young man who had plaque-like lesions similar to the ones I had seen. The course of the disease, however, was subacute, the picture changed much more quickly, and the patient recovered spontaneously after several months. Still another case was published by Kreibich, of Prague (*Arch. Dermat. u. Syph.* 150:243-248, 1926). This was a case of parapsoriasis en plaques in which the hair follicles showed mucinous changes. Of course this could have been an early case of mycosis fungoides. It seems to become clear, then, that there are primary and secondary cases of root sheath mucinosis. There is an idiopathic type with the clinical picture of alopecia mucinosa and a symptomatic type that occurs in reticuloses and lymphomas.

The clinical picture in the case here is a little different from that in the first five cases. Here we have grouped follicular papules rather than plaques. One could almost think of a case of lichen spinulosus. However, the boy at one time had alopecia of the scalp. The hair fell out in a circumscribed area after some weeks. This apparently was not alopecia areata but was related to these other lesions on the back of his neck.

Dr. Herschel S. Zackheim: It is needless to say that the biopsy diagnosis was a complete surprise to me. This, then, is something else to keep in mind when a child, or possibly an adult, presents a scaling alopecia in which the hairs can easily be pulled out and do not fluoresce and when studies for fungi are negative. It also adds another differential to the list of grouped follicular papular eruptions. The small-sized flesh-colored papules

Dr. Robert E. Burns: It seems that x-ray therapy is effective in this condition. Would Dr. Pinkus care to give the rationale?

Dr. Hermann Pinkus, Monroe: X-ray treatment was used on a trial basis in the first case by Dr. W. Macauley. It has been beneficial or curative in several other cases. If this is an infectious process affecting sebaceous gland cells specifically, it might be arrested or cured by knocking out the sebaceous glands temporarily. This can be accomplished by relatively small doses of x-ray therapy.

**Lepromatous Leprosy.** Presented by Dr. Alice E. Palmer and Dr. Stanley Greenberg.

This 31-year-old Filipino woman has been living in the United States since 1954. She was admitted to Grace Hospital on Nov. 9, 1957, with the complaint of general malaise, skin eruption, and fever of 10 days' duration, becoming progressively severer.

The past history was essentially negative.

The family history was negative.

Physical examination revealed an acutely ill woman with a temperature of 104 F. There were erythematous nodular lesions predominantly on the extensor surfaces of arms and legs. There were several on the face and back. These nodules were tender and varied from 1 to 4 cm. in diameter. In both axillae and in the left inguinal region large tender lymph nodes were palpated. The remainder of the examination was essentially negative.

Laboratory findings revealed Hb. 12.2 gm.; WBC 21,200, with 87% polymorphonuclear cells and 13% lymphocytes; albumin 3.5 gm. %, and globulin

2.9 gm. %. Urinalysis was negative; serologic test for syphilis was negative; erythrocyte sedimentation rate was 92 mm. in an hour. Chest x-ray, E. C. G., antistreptolysin titer, and L. E. preparations were all normal. Both nasal and skin smears showed acid-fast saccule.

Biopsy of the skin: Acid-fast stains show large number of acid-fast saccules in the corium; they are small and slender. Some are slightly bent and show irregular staining.

Treatment: Cortisone, 75 mg. was given orally every six hours. The response was dramatic. Symptoms disappeared and temperature returned to normal in 24 hours. Nodular lesions gradually faded. Upon confirmation of the diagnosis of leprosy patient was given Diasone, 0.3 gm. per day. On Nov. 20, 1957, cortisone was discontinued, and the patient had prompt recurrence of fever, malaise, and skin lesions. Cortisone was resumed, and arrangements were made for her transfer to the U. S. Public Health Service Hospital at Carville, La.

### Discussion

DR. ALICE E. PALMER: This patient has been troubled on and off for the past several years with vague complaints. She was managed in a large allergy clinic for recurrent blotchy erythematous macules over the arms and hands for about two years. No favorable results were obtained. In September, 1957, she began feeling ill and thought she had the "flu." The Student Health Service at the University administered penicillin. The malaise persisted, and in about 30 days she had developed extensive erythema nodosum. A diagnosis of "penicillin reaction" and possible rheumatic fever was then made. Her temperature was of a septic type and ranged from 101 to 104 F. She collapsed at the Health Center and was hospitalized.

On examination, she presented large deep purple painful erythema nodosum primarily over the tibiae and forearms, although there were scattered smaller lesions over the thighs and upper arms and there was one on the face and one on the upper back.

Diagnostic procedures included the cutting-down technique to look for mycobacterium leprae. This procedure was repeated in several areas, even in "normal" skin. All the cuts produced serum which was loaded with bacilli (i. e., more than 4 per high-power field). Biopsy also showed the classic acid-fast bacilli deep in the corium. Nasal smears were positive.

In this type of case, leprosy manifests itself as an intense bacillosis which is really universal. This is the prelepromatous stage of the disease. Only later, when the body begins an attempt to "organize" about these bacilli, do the visible classical lepromata appear.

These changes can be prevented by the administration of steroids. In this case, body reaction was prevented by the use of cortisone. All her nodose lesions faded completely. Then specific antibacillary medication is added, such as Diasone.

This patient is now recovering. We feel that the early use of the anti-inflammatory drug will prevent any disfiguration in this patient. This patient is interesting in that her case points up the necessity of thinking broadly even in all patients who present what might seem to be classic eruptions—in this case, "erythema nodosum." By early diagnosis we can prevent a lifetime of disability in some of these persons.

DR. MERLE HAANES, Pontiac: The degree of hyperergy at this early stage is extremely severe. At first thought one might fear steroids for the same reason one avoids them in pulmonary tuberculosis, but, since this not a localized lesion and bacteremia is already present, with coverage by suitable chemotherapy steroids become the treatment of choice.

DR. CLARENCE S. LIVINGOOD: At this acute early stage, leprosy may well resemble Weber-Christian disease and proof of the correct diagnosis may be extremely difficult.

The following cases were presented by DR. ALICE E. PALMER and DR. STANLEY GREENBERG and GRACE HOSPITAL STAFF.

**Lichen Planus Acute.**

**Adenoma Sebaceum.**

**Onychomycosis?**

**Port-Wine Stain—Treatment Problem.**

**Granuloma Annulare.**

**Parapsoriasis.**

**Keratoses, Etiology Undetermined.** Presented by DR. HAROLD PLOTNICK.

**Dermatitis Medicamentosa (to 666).** Presented by DR. STANLEY GREENBERG.

**Weber-Christian Disease.** Presented by DR. GEORGE B. SEXTON, London, Ontario, Canada.

## THE LOS ANGELES DERMATOLOGICAL SOCIETY

**Kenneth L. Stout, M.D., President**
**Floralou Kettenbach, M.D., Secretary**

**Jan. 8, 1958**

**Metastatic Malignant Melanoma.** Presented by Dr. Paul D. Foster.

The patient is a 61-year-old woman of Irish-English descent.

Significant Past History: In 1928, a hysterectomy was done for prolonged bleeding and carcinoma of the uterus was the diagnosis.

Significant Family History: Mother died, age 61, carcinoma of the uterus; father died, age 49, carcinoma of the lip with metastasis.

Present Illness: In 1951 she noted a "mole" on the left calf. For the next two years this reddish-brown lesion grew until it reached a size of a silver dollar. At this time she sought medical treatment from a surgeon, and the entire area was removed by wide excision followed by a skin graft from the thigh. During the same hospitalization, in May, 1953, a left inguinal dissection was performed, and about a week later, according to the patient, a "tumor" was removed from the stomach.

From 1953 until 1955 the patient remained well.

At this time a shower of small lesions appeared on the left thigh. She was given x-ray therapy to these areas, but, despite therapy, the condition progressed. She states that following irradiation the area from which the graft had been removed sloughed out.

For the next two years no treatment was given. In February, 1957, this patient was first seen in our office with innumerable lesions.

Description of Current Dermatosis: The left thigh is peppered with innumerable sessile, indurated, shiny papules of a reddish-brown to deep-red hue. These varied in size from pinpoint to larger than a pea; some were discrete while others were coalesced, in a few instances, in annular or linear configuration. On the posterior aspect of the left calf there was a saucer-shaped palm-sized excavated scar. On the posterior aspect of the left thigh, the site of the removal for the graft was seen.

Biopsy Findings: Malignant melanoma.

Treatment and Results: The larger and more bulky lesions have been excised. Some lesions have been subjected to irradiation with the Phillips Contact x-ray unit. It was felt that x-ray gave the most satisfactory results. The patient's treatment has been rather irregular. Recently she reappeared with a grapefruit-sized, indurated, tender, hot inflammation of the medial-lateral aspect of the left thigh. This has been treated with penicillin and has been undergoing involution.

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### Discussion

Dr. Molleurus Couperus: This is an interesting case in several aspects. First of all, the lesions on the thigh which are apparently metastatic melanomas are all nonpigmented, which is unusual. I presented a patient here about five years ago who had a primary tumor removed from the ankle and subsequently developed about 200 metastases on the same extremity, and, of the approximately 200 metastases there were about 4 nonpigmented lesions and the others were pigmented. In this patient today, I was unable to find a single pigmented lesion. In the biopsy specimens the histopathological picture is unquestionably that of a melanoma. The second thing that strikes me as an unusual feature is that one of the lesions responded to contact x-ray. I treated three metastatic lesions in my patient, each lesion receiving 6000 r at one sitting, and, although necrosis followed, the melanoma was still present when the area was excised, about four or five weeks later.

Dr. Louis H. Winer: The nonpigmented melanoma frequently forms pigmented metastases when it metastasizes to an internal viscus. I would advise checking the urine for melanin. In Germany, doctors are using necrotizing doses of roentgen rays in the treatment of melanoma, which frequently result in more suffering for the patient than his melanoma. The melanoma cells, as a rule, are very roentgen-ray resistant.

Dr. J. Walter Wilson: A nonpigmented melanoma cell is more anaplastic than a pigmented one, tending the embryonic phase, and therefore would naturally be expected to be more sensitive to radiation.

Dr. Walter Nickel: At the combined meeting with the San Diego Dermatological Society about 8 or 10 years ago, a woman was presented on two occasions with malignant melanoma on her leg which was excised followed by metastases to the leg—just as this woman has. When these lesions became so big that she could not walk around any more, the larger lesions were excised. She lived for about 14 years and finally died of malignant metastatic melanoma. She had had a groin dissection at the time of the original diagnosis, and possibly the fibrosis in the groin from the surgery

which had been done accounted for the fact that the malignancy was held in abeyance and limited to that leg for such a long period of time. Doctor Becker and I were talking about xeroderma pigmentosa and malignant melanoma. We had a girl with xeroderma pigmentosa who finally went on and developed malignant melanoma on her leg and for whom the same treatment with groin dissection was carried out. She lived for about six years following the dissection in the groin, and her lesions also remained limited to that leg until just before her death. There is either some natural blocking or there is some artificial blocking in the form of fibrosis that holds these lesions in check.

DR. A. FLETCHER HALL: This case is a good reminder to us of the capriciousness and unpredictability of malignant melanoma. Here is a woman who had a lesion for two years before it was excised. It was excised (widely and deeply, from the appearance of the wound) and then was perfectly clear for a matter of two years; then myriads of metastases appear, but they remain limited to her leg and she still appears to be in good health. I cannot conceive of sufficient fibrosis occurring following a groin dissection to block the passage of melanoma cells without giving rise to at least *some lymphedema.* I do not think that can be an operative mechanism in limiting the metastases.

DR. LOUIS H. WINER: In melanoma there is frequently a bizarre configuration of metastatic lesions due possibly to blockage of the regional lymphatics and resultant hypostatic seeding. The superficial lymphatics in the skin are very reticulated, and thus the pattern assumed is corymbiform.

DR. S. WILLIAM BECKER: Microscopic examination of the primary tumor might be of assistance in evaluation of the process. The short period between local removal with lymph node resection and recurrence suggests a longer duration than is given in the history. Recurrence of melanoma only between the primary tumor and the groin illustrates the concept of proponents of lymph node removal that recurrence will be largely local and more susceptible to treatment. Response to roentgen therapy shown by the treated metastatic tumor may indicate that the neoplasm falls in the 2% of melanomas which F. W. Stewart (Radiosensitivity of Tumors, *Arch. Surg.* 27:979-1064, 1933) stated have some degree of radiosensitivity. Spontaneous regression which many of the tumors seem to be undergoing has been reported rarely (Sumner, W. C.: Spontaneous Regression of Melanoma: Report of Case, *Cancer* 6:1040-1043, 1953). The present European method of treating melanoma with a cauterizing dose of roentgen rays may owe its success to early diagnosis and treatment before the tumor has spread beyond the irradiation field. Surgical excision usually removes a more extensive area than is exposed to roentgen irradiation.

DR. CLEMENT E. COUNTER: I would like to ask Dr. Couperus about the case he treated. Was the lesion he treated with x-rays a pigmented lesion or one of the few nonpigmented lesions?

DR. MOLLEURUS COUPERUS: Those were pigmented metastases. There were very few nonpigmented lesions in that patient. To me, it appears possible that occasionally a patient who has malignant tumors and who is subjected to a prolonged high fever in the course of a disease might experience a disappearance of his malignancy. I had a patient with advanced mycosis fungoides in the tumor stage who developed pneumonia with a high temperature, and all the lesions of mycosis fungoides disappeared. The patient died several months later, and at autopsy there was no evidence left of the mycosis fungoides. This patient of Dr. Foster's may have had a partial disappearance of tumors through fever. The question arises whether it might not be a real contribution to dermatology if this patient could be treated experimentally with hyperthermia generally, or perhaps locally to a group of lesions.

DR. J. WALTER WILSON: Whether or not a cell is sensitive to radiation is a purely relative matter. There certainly is a dose of x-ray that no living cell can survive. Therefore, what I choose to call a "charring" dose of x-ray is capable of removing even a pigmented metastatic melanoma. If the x-ray penetrates deep enough and wide enough, it is as effective as a soldering iron.

DR. MURRAY ZIMMERMAN: When I talked to the Germans the rationale of therapy was a little different. They feel that surgery, even biopsy, may jolt loose some malignant cells which will spread easily in a melanoma. With this idea, they give, as you said, very large doses of x-ray. After 20,000 r of contact therapy in one dose to the area, they immediately move the patient to surgery and excise the melanoma plus the irradiated margin, plus a surgical margin around the irradiated area, just as fast as they can get the patient from the x-ray table to the surgery table. They feel that any cells shaken loose by the surgery will have had a lethal dose of x-ray and will be unable to reproduce as metastases.

**Case for Diagnosis: Eosinophilic Granuloma; Letterer-Siwe Disease (Nonlipid Reticuloendotheliosis); Nevoxanthoendothelioma?** Presented by DR. MEYER BERKE.

This 4-month-old white boy was first observed, at the age of 6 weeks, to develop flesh-colored, erythematous, multiple, nodular lesions on the scalp, trunk, and lower lip. These have gradually increased in number and size. One of these lesions,

on the scalp, was excised, and the pathologic diagnosis of eosinophilic granuloma was suggested. The patient has been under the care of a pediatrician. Laboratory studies have thus far failed to show systemic evidence of Letterer-Siwe or Hand-Schüller-Christian disease. The baby has apparently developed normally and shows no evidence of constitutional disease. However, some of the lesions have been irritated and are crusted and very tender.

Examination of the skin revealed multiple flesh-colored to erythematous nodules of varying sizes. Some of these were umbilicated with crusted centers. They were chiefly located on the scalp, lower lip, trunk, and buttocks.

A complete bone survey was reported as normal. RBC, 4,300,000; WBC, 9800; Hb., 11.75; Eos., 1%; Segs., 18%; L., 80%; M., 1%.

### Discussion

DR. WALTER R. NICKEL: In looking at the microscopic slide and considering that the rest of the examinations were negative, I believe this is juvenile xanthogranuloma or nevoxanthoendothelioma. Dr. Helwig points out in his discussion that you do not always have giant cells present in making the diagnosis of juvenile xanthogranuloma. The microscopic section does not show any giant cells. So, the xanthomatous element of this disease to the point of producing giant cells is not necessary for the diagnosis.

I remember that Meyer Berke, about a year ago, presented a case of urticaria pigmentosa with a bullous nodular lesion which looked somewhat similar to this case. I am sure that he has considered doing a mast-cell stain in this case as well —even though the result will probably be negative.

DR. LOUIS H. WINER: These xanthomatous lesions on infants are very frightening and alarming to their parents. They sometimes cover the entire body. Two fatal cases reported by Dr. Herman Beerman (Histopathological Round Table, American Medical Association Meeting, Section on Dermatology, Atlantic City, 1955) showed involvement of the eye, testes, and brain. They are very rare. Dr. Elson B. Helwig (Course in Granuloma, American Academy of Dermatology and Syphilology, 1957) doesn't believe the cause of death in one of these infants was due to the xanthogranuloma, but rather to the child's malnutrition. My impression has been that these lesions always disappear spontaneously.

DR. MEYER BERKE: Previously one of the scalp nodules had been biopsied, and the specimen was sent to Dr. French, of the Pathology Department, University of Michigan, who interpreted the histopathology as suggesting eosinophilic granuloma. Physical examination was essentially normal, and a bone survey was reported to be negative. Many of the lesions were umbilicated and, despite the pathologic report, were suggestive of large lesions of molluscum contagiosum. However, repeat biopsy of another lesion showed the same histopathologic change as the original tissue, except that eosinophils were far less numerous. Clinically in the past three to four weeks more of the lesions have changed from flesh-color to a xanthomatous hue. Considering all factors thus far, the most likely diagnosis would appear to be xanthogranuloma rather than reticuloendotheliosis.

**Clear Cell Hidradenoma.** Presented by DR. NORMAN E. LEVAN.

**Case for Diagnosis: Possible Clear Cell Myoepithelioma; Possible Eccrine Spiradenoma?** Presented by DR. LAURENCE J. UNDERWOOD.

**Pyoderma Gangrenosum.** Presented by DR. SAMUEL AYRES JR. and DR. SAMUEL AYRES III.

**Case for Diagnosis: Xanthoerythroderma Perstans; Parapsoriasis en Plaque Broeq?** Presented by DR. S. WILLIAM BECKER and (by invitation) DR. DONALD G. LINDSAY.

**Case.** Presented by DR. MAXIMILIAN E. OBERMAYER.

**Radiodermatitis of the Face.** Presented by DR. ANKER K. JENSEN.

## METROPOLITAN DERMATOLOGICAL SOCIETY OF NEW YORK

**Milton B. Sloane, M.D., President**
**Wilbur B. Hurlbut, M.D., Secretary**

**Jan. 16, 1958**

**Lymphoblastoma.** Presented by DR. ANTHONY N. DOMONKOS.

A white man, aged 48 has had recurring lesions on the left arm and left popliteal space for the past six years. These lesions have been biopsied a number of times.

Description: At the present time, the patient has infiltrated brown nodules, some arranged in arcuate fashion on the left arm.

Laboratory examination: All blood cell counts up to the present time have been within normal limits. The same is true of sedimentation rate and blood platelet counts.

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Biopsies: May 8, 1952: "Throughout the cutis is a tremendous cellular infiltration. The overlying epidermis is slightly acanthotic and flattened, but otherwise shows no important change. In some areas, the type of cell cannot be determined. In the upper portions, there are various types of cells including small round cells, wandering connective tissue cells, and some epithelioid cells. An occasional mitotic figure can be seen.

"Diagnosis: Lymphoblastoma."

May 15, 1952: "This cutaneous lesion reveals an epidermis which is not remarkable. The entire cutis, however, is massively infiltrated by relatively small mononuclear cells. These appear to be of lymphoid derivation. Their nuclei are small, round, and hyperchromatic. The lesion is either a round-cell lymphosarcoma or a leukemia. I would suggest that the patient have a careful hematologic investigation.

"Diagnosis: Lymphoblastoma."

Sept. 28, 1954: "Sections of a cutaneous lesion from the 'left upper arm' disclose a thinned, somewhat hyperkeratotic, epidermis. Infiltrating the cutis are numerous mononuclear leukocytic elements. These are relatively large and morphologically suggest reticuloendothelial cells. This infiltration comes up to the epidermis but does not involve it. Focal infiltration of similar cells is seen in the deeper aspects of the specimen. I should have said that the cells in many places tend to simulate lymphocytes. The lesion is evidently a lymphoblastoma and probably should be classified as a lymphosarcoma.

"Diagnosis: Lymphosarcoma."

Course: This patient has responded remarkably well to x-ray therapy. Within the past two years, most of the recurring lesions have been treated with Meticortelone suspension injected into the lesions. One injection of a lesion has usually been enough to cause complete involution of the lesion. The involution usually occurs within a period of two weeks. Two weeks ago, the patient had so many lesions on his arm that it was not thought feasible to inject all of them with Meticortelone because of the possible systemic effects, and, therefore, 100 r was given to the lesions on the left elbow and arm. This was at 100 kv. with a half-value layer of 1.3 mm. Al.

## Discussion

Dr. Royal M. Montgomery: A point of interest to me is the fact that the prednisolone injected subcutaneously was of help in this disease. I have used this injection in a variety of diseases, but I have frankly never heard of it being used in mycosis fungoides. I am glad to learn that it resolved an individual lesion.

Dr. Thomas N. Graham: I wondered just how much x-ray treatment the patient has had and to what degree it accounts for his improvement.

Dr. Wilbur B. Hurlbut: I did not clearly understand whether Dr. Domonkos presented this case as mycosis fungoides or lymphosarcoma.

Dr. George C. Andrews: It has been interesting to me to see this case develop through the years, because, at first, the histology was that of a rather benign process classified as lymphocytoma, and it was doubted whether it would develop into a lymphoblastoma. But it has progressed, in spite of being cleared up temporarily by various remedies. The histology has become more and more definitely that of lymphoblastoma. The evolution has been very slow.

Dr. J. Lowry Miller: I was under the impression that you presented this patient as an example of lymphosarcoma. This is purely theoretical, and contrary to accepted teaching, but I wonder if exposure to light may be a factor. We have a patient who had biopsies performed on five different occasions with reports of leukemia cutis. He used to have recurring lesions on his back. He was a great sun addict. We hit upon the idea of not letting him expose himself to sun, and, for the last five years, he has remained free of these lesions. I noticed the fact that the man had on the upper arm an area that was exposed to sun, and he also had some on the back of his knees. Frankly, I have never heard the idea presented before, but I thought that it might be of some significance in this relatively benign type.

Dr. Alex W. Young Jr.: I should like to ask if any controls were used. The precipitation of an inflammatory reaction, perhaps nonspecific in a case such as this, might well have the same results as the injection of Meticortelone. I should also like to ask Dr. Domonkos what his technique for injection is, as I have found it sometimes very painful.

Dr. Irving Abrahams: We had a patient at the Presbyterian Hospital, who has been treated with other means since, who had a very severe, widely distributed mycosis fungoides and was given large doses of Meticorten by mouth and had temporary remission. I think that was also reported by Dr. Lewis, in one or two cases. It was just temporary.

Dr. Anthony N. Domonkos: We injected Meticortelone suspension into some of the lesions in another case, and there was some involution. The amount of Meticortelone that we can inject at any one time is limited; that is, we try to stay within limits of about 1.5 cc. for a total injection. It is approximately 38 mg. Undoubtedly, there is a considerable amount of absorption, and it could have a systemic effect.

There has been one recent biopsy. Of three biopsies, one was reported as lymphosarcoma and

two as lymphoblastoma, one by Dr. Sachs and one by Dr. Machacek.

DR. WILBUR B. HURLBUT: The one in 1954 was lymphosarcoma.

DR. ANTHONY DOMONKOS: In regard to sunlight, we have had several patients with mycosis fungoides whom we have treated with weekly doses of ultraviolet treatment at the clinic, with marked amelioration of symptoms, especially that of itching. A woman who had mycosis fungoides on the arms went for years with nothing else but ultraviolet treatment. She got relief from her symptoms of itching.

This patient presented tonight has not been exposed to sun; we have had a chance to observe him over a period of six years, and there was no exacerbation of lesions when he did get sunburned, that is, exposed to the sun during the summertime.

DR. THOMAS N. GRAHAM: I think you said that he had had some treatment with x-rays?

DR. ANTHONY DOMONKOS: Oh, he has received a considerable amount of x-irradiation. I would judge that he might have received as much as 2000 r in that area, in doses of 100 r at weekly intervals, on and off over the six-year period.

DR. MILTON B. SLOANE: I think that Dr. Young asked about your technique.

DR. ANTHONY N. DOMONKOS: These lesions are very easily given injections. I use a 24-gauge needle, as the 26-gauge needle will not let the particles of suspension go through and they will plug up the syringe. Just inject it into the lesions.

**Pigmented Basal-Cell Epithelioma.** Presented by DR. ANTHONY N. DOMONKOS.

A Puerto Rican man aged 45 was first seen at the Vanderbilt Clinic in October with an ulcerated lesion covering at least one-half of the left side of the nose. There were also several indurated areas with marked pigmentation. At the left ala nasi, within the lesion, was a depigmented area about 1 cm. in diameter. A diagnosis of pigmented basal-cell epithelioma was the clinical diagnosis. This was confirmed by the histopathological findings also.

The involved area was treated by giving 300 r daily, for a total of 3000 r. This was at 100 kv. unfiltered, half-value layer 0.8 mm. Al. There was marked erythema and pigmentation after the conclusion of the roentgen therapy. However, there still remain granulomatous lesions in this treated area.

Because of the lack of rapid response to radiation therapy and because the patient has several small nodular lesions on the left temple, a biopsy of a lesion was performed on the left temple on Nov. 12, 1957. A diagnosis of acne and chronic inflammatory dermatosis, rosacea (?) was reported.

Biopsy: The biopsy of the lesion on the nose was reported as follows: These sections of a cutaneous neoplasm of the nose reveal a lesion which is surmounted by a thick keratin layer and a fibrinopurulent exudate. In the cutis examination are revealed aggregates, some of them cystic, of neoplastic epithelial cells. The tumor cells are similar morphologically to basal elements. Some of them are melaniferous. Diagnosis: Pigmented basal-cell epithelioma.

The biopsy from the left temple lesion was reported as follows: Sections of a lesion of the left temple reveal a slightly edematous epidermis, and in some sections of a large hair follicle there is contained a comedo. In the cutis there are perivascular infiltrations of mononuclear leukocytes, some of which are plasma cells. Some of the vessels are dilated. In some sections one could identify sections of nerves which, however, did not show changes suggestive of leprosy. The lesion is essentially one of chronic inflammatory nature but is not granulomatous. The histologic changes are not characteristic of leprosy. Are there any clinical stigmata of leprosy, such as hypoesthesia? At any rate, studies with acid-fast stains will be done. (These have not been reported as yet.)

**Discussion**

DR. JUAN LARRALDE: From the clinical picture, I should think of tuberculosis cutis, and I think that another biopsy of that lesion should be done.

DR. GEORGE C. ANDREWS: The dosage of x-rays which was given was below the usually accepted cancerocidal dose, which would be about 5000 r. This was a total of about 3000 r, probably because the area was fairly large. But the lesion did not respond to the x-ray treatment. It was radioresistant. I believe that it should be treated by some other type of therapy.

DR. ANTHONY N. DOMONKOS: How?

DR. GEORGE C. ANDREWS: I think that it would be fairly simple for a surgeon to excise it and transpose a little flap from the cheek onto the nose.

DR. J. LOWRY MILLER: I think that you would get a beautiful result with electrodesiccation and curettage. I grant that you will get a whitish area, but, in him, it is of no great significance. It is a simple procedure and, if you fail, you could still do the other procedure, namely, plastic, with a flap.

DR. ANTHONY N. DOMONKOS: I presented this patient mainly because of the slightly disturbing histologic report and the fact that we did think of the possibility of leprosy on the forehead, which certainly was suggested in the histologic report itself. There is no doubt about the fact that this man had a pigmented basal-cell epithelioma of the nose, a clear-cut picture.

I seriously considered desiccating the entire area, and the only reason I did not do it was that, as we all know, x-ray therapy on pigmented basal-cell epitheliomas will take away the epithelioma but the pigment will remain. However, I was deterred from electrodesiccation mainly because if I were to desiccate this entire lesion there would remain a marked whitish area which would be disfiguring. I therefore chose to treat this by x-ray. There was a marked reaction, with vesiculation and marked pigmentation.

Despite the fact that 3000 r is a rather small dose, I felt that he had had enongh of a reaction to take away the epithelioma.

**Sarcoid.** Presented by DR. ROYAL M. MONTGOMERY.

**Contact Dermatitis Due to Thermo-Fax Duplicating Paper.** Presented by DR. ANTHONY N. DOMONKOS.

**Adenocystic Basal-Cell Epithelioma.** Presented by DR. ANTHONY N. DOMONKOS.

**Penicillin Eruption.** Presented by DR. WILBUR B. HURLBUT.

**Lichen Planus.** Presented by DR. WILBUR B. HURLBUT.

**Alopecia.** Presented by DR. ANTHONY N. DOMONKOS.

## METROPOLITAN DERMATOLOGICAL SOCIETY OF NEW YORK

**Feb. 20, 1958**

**Comedone Nevus.** Presented by DR. CHARLES F. POST.

A 4-year-old white girl was born with a lesion of the forehead. It has grown pari passu with general body growth. It has been asymptomatic.

Examination: On the forehead, above the eyebrow level to the hairline, is an irregularly shaped lesion consisting of numerous discrete retracted follicular orifices filled with comedones.

Treatment: Comedones have been expressed on frequent occasions, and sulfur-resorcin lotion has been applied nightly. A cleansing solution has been used to remove the material from the pores, and treatment with carbon dioxide slush has been used over a period of three months, with no objective improvement.

Patient is presented for treatment suggestions.

### Discussion

DR. GRAHAM: I suggest x-ray therapy, since the lesion seems to be a nevus involving the sebaceous glands. If this therapy does not entirely clear the eruption, it will at least improve it.

DR. HURLBUT: I was wondering as to whether the best form of treatment would be dermabrasion or surgical excision. The pathology is probably too deep for dermabrasion. Surgical excision later on could be done in two stages, and it probably would result in a fine linear scar which would be preferable to the nevus.

DR. KRAUT: These lesions usually present dilated follicles in the skin, which are filled with keratinous material. Most of the cases that have been presented in this country and in England have shown considerable perifollicular inflammation, in most cases going on to cyst formation and scarring. I think that Dr. Post has kept this case in really excellent condition with the treatment he is now applying.

DR. SPOOR: My thoughts are to wait until the child is older and then eventually do the surgical repair, which, I think, will be necessary. I do not question the efficacy of x-ray therapy, but I would be a little bit hesitant to use it in this particular case.

DR. YOUNG: The treatment of choice is probably excision. However, this step should be deferred until later.

DR. BAKER: These nevi are very much deeper than you think. They appear to be very superficial, but this type of linear nevus is always a good deal deeper than it appears, and, if you go to remove them, you find you have quite a problem, and you are going to have a lot of scarring. I think that it might be wise to wait a year or two and see what happens to the lesion before you do too much surgery, unless the nevus tends to get larger.

**Urticaria Pigmentosa.** Presented by DR. CHARLES F. POST.

**Case for Diagnosis.** Presented by DR. ALEX W. YOUNG JR.

**Urticaria Pigmentosa.** Presented by DR. WILBUR B. HURLBUT.

**Dermatitis Herpetiformis.** Presented by DR. ALEX W. YOUNG JR.

**Seborrheic Dermatitis; Seborrhea Congestiva-Hebra?** Presented by DR. ALEX W. YOUNG JR.

**Contact Dermatitis Due to Thermo-Fax Paper.** Presented by DR. CHARLES F. POST.

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## NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILOLOGY

**Jack Wolf, M.D., Chairman**
**L. P. Barker, M.D., Secretary**

**Jan. 7, 1958**

**Colloid Degeneration of the Skin.** Presented by DR. DAVID BLOOM.

From: New York Skin and Cancer Hospital Unit of University Hospital; service of Dr. Nathan Sobel.

History: A man aged 72 presents an eruption on the forehead which has been present for two years. It consists of yellow nonindurated plaques composed of individual milium-like lesions. The eruption is most marked on the sides of the forehead. There are no subjective symptoms.

Biopsy examination done by Dr. Charles Miller was reported as follows: "The epidermis is normal. In the upper cutis there are globular masses of degenerated collagen fibers, which show slightly basophilic staining with hemotoxylin-eosin. Polychrome staining excludes amyloid degeneration. Diagnosis: Colloid Degeneration."

While "colloid milium" is characterized by small, round, yellowish nodules, so-called "colloid degeneration" of the skin presents a yellowish plaque.

Some authors believe that colloid, like amyloid, represents a deposit and not a product of collagen degeneration. Colloid is a complex albuminous substance. Its exact chemical nature has not been determined. That colloid degeneration is not just a senile change is proved by the fact that the condition has been reported in young people.

The precipitating fact in this patient is, I believe, an excessive exposure to sun and weather, for he has been a bricklayer for many years and, for the past four years, he has done quite a bit of fishing.

**Reticulum-Cell Sarcoma.** Presented by DR. ORLANDO CANIZARES.

From: The Department of Dermatology and Syphilology of the New York University Post-Graduate Medical School (Dr. Marion B. Sulzberger, Chairman) and the Service of Dermatology and Syphilology of Bellevue Hospital (Dr. Frank C. Combes, Chief of Service).

History: This patient, a 65-year-old Negro man, presents multiple nodules and tumors scattered over the abdomen, lower back, lower extremities, and forearms. The lesions vary from 1 cm. to 8 cm. in diameter. Most of the lesions apparently involve the dermis; a few even have ulcerated through the epidermis. Others on the abdomen and right forearm seem to be entirely subcutaneous. Most of the tumors are remarkably hard, discrete, and nontender. The more superficial ones have a dusky, bluish-red hue. But, on the right sole there is a soft swelling 5 cm. by 7 cm., which is tender on deep pressure and makes walking painful. A large tumor on the left calf is deeply ulcerated and has a black, necrotic, foul-smelling base. On the legs there are several mummular, hyperpigmented, slightly scaly, superficial scars, which, according to the patient, represent spontaneous resolution of nodular lesions. The superficial lymph nodes do not seem to be significantly enlarged. The liver is enlarged 1 fingerbreadth below the costal margin, and the tip of the spleen is barely palpable. The very first lesion was an ulceration on the left ankle which appeared about three years ago, and that lesion is now a healed scar. New nodules have developed at a fairly steady rate since then. Systemic complaints consist of anorexia, moderate weight loss, and weakness. On the ward the patient has run an irregular fever, with temperature to 103.5 F. The patient has been treated with mechlorethamine hydrochloride intravenously, 0.4 mg. per kilogram divided into two equal doses, given on Jan. 2 and Jan. 3, 1958.

As regards laboratory studies, a biopsy specimen of a nodule on the right thigh was read by Dr. William Director as reticulum-cell sarcoma. Bone marrow examination on Dec. 27, 1957, disclosed an increase in the myeloid/erythroid ratio, with increased plasma cells, lymphocytes, platelets, megakaryocytes, and atypical monocytes; this picture was considered by Dr. A. Wiener to be "not diagnostic, but consistent with a malignant disease." Several complete blood cell counts, urinalyses, a chest plate and bone series, blood chemistry determination, and liver function studies all have been within normal limits. Serum electrophoretic pattern showed a moderate decrease in $\gamma$-globulin.

### Discussion

DR. VICTOR H. WITTEN: I would like to discuss the question of radiation for this patient and for this disease. While treatment with x-rays was not listed on the presentation sheet, as I recall, the patient said that he had had considerable x-ray in the past. That may be the reason that no attempt was made to give the details of radiation delivered to the many individual lesions.

As a point of interest, I would like to tell you about a patient with similar involvement, though

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less extensive. In the attempt to find the most effective quality of radiation for the treatment of this patient's lesions of reticulum-cell sarcoma, various lesions were treated differently in the radiotherapy section of the Skin and Cancer Unit and of the University Hospital (New York University Post-Graduate Medical School). Rather than giving 300 r per treatment of radiation of 4 mm. Al half-value layer, we asked that the radiologists cooperate with us in standardizing treatment and that they give but 50 r with their machine at 130 kv. to one lesion. Another similar lesion was given 50 r at 100 kv. and a half-valve layer of 0.9 mm. Al. A third similar area was treated with the specially designed unit installed in the Skin and Cancer Clinic to give teleroentgen therapy. With this unit, 50 r was delivered at 50 kv., 0.2 mm. Al half-valve layer. After four such treatments, the lesion treated with conventional dermatologic radiation responded the best. I think that this experience indicates that our conventional form of dermatologic x-ray can be depended upon to achieve results. Of course, there will be cases where some filtration will be desirable or where high-voltage machines delivering even harder radiation will be necessary.

DR. JESSE A. TOLMACH: I observed this patient at the New York Skin and Cancer Clinic on several occasions. Serologic tests for syphilis were positive, and there was a temporary response to treatment with penicillin. New lesions continued to appear, and drug eruption and deep fungus infection were considered. Curiously, there was evidence, too, of spontaneous healing. An earlier biopsy specimen was not particularly informative, but a more recent one was reported as reticulum-cell sarcoma.

DR. EUGENE T. BERNSTEIN: I think Dr. Wiener examined the patient from a hematopoietic standpoint and did not find a criterion for this being a lymphoblastoma but said there is some diagnosis of malignancy. Is this correct?

DR. JACK WOLF: The history reads in part: "The picture was considered by Dr. A. Wiener to be 'not diagnostic but consistent with a malignant disease.' " That was on bone marrow examination.

DR. EUGENE T. BERNSTEIN: I believe this type of sarcoma is an expression of some disease in the hemopoietic system. These reticulum cells are big juicy cells. This is the first time that I have seen such a case. On clinical grounds the case looked to me just like a Kaposi's sarcoma. This is a very interesting case, if we should rely only on the histologic examination. There must be some intrinsic difficulties. While there are cases of reticulum-cell sarcoma without any skin changes, I do not think such cases are seen very often.

DR. ORLANDO CANIZARES: The interesting thing is the unusual clinical picture. As we see this patient tonight with the purple nodules and the confirmatory biopsy, the diagnosis is very easy to make, but the dermatologists who saw him about three or four months ago at the Skin and Cancer Hospital were puzzled by the picture. When he came to Bellevue, we were also puzzled. The lesions were very inflammatory, pyogenic in appearance. They seemed to start deep in the subcutaneous tissue. We thought of the possibility of a panniculitis. One of the biopsy reports stated that the process was pyogenic. That shows that the clinical picture of the case is very puzzling. As Dr. Tolmach mentioned, some of the lesions seemed to heal spontaneously. There are scars on the leg where the process healed spontaneously and then became ulcerated and finally presented the picture which is present today.

**Acropigmentation.** Presented by DR. DAVID BLOOM.

From: New York Skin and Cancer Hospital Unit of University Hospital; service of Dr. Nathan Sobel.

History: A Negro girl aged 19 presents hyperpigmentation on the dorsum of the right fifth metacarpophalangeal joint, on the dorsum and the flexures of all the first phalangophalangeal joints, and over the dorsum of the distal phalanges of the fingers. The toes show similar hyperpigmentation.

The hyperpigmentation appeared first four years ago on the flexures of the finger joints and spread quickly to the other areas.

No other member of the family is affected.

### Discussion

DR. DAVID BLOOM: Several years ago we saw, at the Skin and Cancer Clinic, a child with a similar pigmentation. At that time, Dr. Kleeberg called our attention to the fact that this condition was described as "Spitzenpigmentation" (acropigmentation) in Jadassohn's "Handbuch" (Vol. 4, Pt. 2, p. 626). The patient presented tonight is the second such case to come under my observation. The literature in regard to this condition is scanty. The term "acropigmentation" was coined by Thomas (*München. med. Wchnschr.* 70:1102 [Aug. 17] 1923; *Deutsche med. Wchnschr.* 50:1479 [Oct. 24] 1924). According to this author physiologic pigmentation on the dorsum of the fingers, less on toes, is seen already in the fetus of six months' of age. In the newborn this pigmentation is covered by the red color, but the pigmentation generally becomes distinct about the middle of the first year, increases in intensity up to the third and 4th year and then begins to lessen in intensity after the 6th year of life. The acropigmentation is considered as a physiologic manifestation caused by phylogenetic hereditary conditions. Adachi

(*Ztschr. Morphol. u. Anthropol.* 6:1, 1903) calls attention to the fact that in monkeys normally there is marked pigmentation on the dorsa of the hands extending to the finger tips. He considers this acropigmentation analogous to the Mongolian spots which also have a tendency to regress in older children.

Our patient is unusual, for she developed the hyperpigmentation over the knuckles and particularly over the distal phalanges at the age of 15.

**Foreign-Body Granuloma.** Presented by DR. SAMUEL B. FRANK.

From: The Department of Dermatology and Syphilology of New York University-Post Graduate Medical School (Dr. Marion B. Sulzberger, Chairman) and New York Skin and Cancer Hospital Unit of University Hospital.

History: Patient is a 16-year-old white boy who presents a lesion on the right knee of three years' duration. Patient states that the lesion followed a trivial fall on pebbles in the street. There is an association of this condition with swimming-pool activity.

Prior to being seen at the Skin and Cancer Unit on Nov. 6, 1957, the patient had been treated, by a dermatologist, with x-ray therapy (total of 600 r given in fractional doses from Nov. 25, 1955, to Feb. 16, 1956). A biopsy report of "probably dermatitis vegetans" was obtained during this period. The lesion also received $CO_2$ therapy.

Patient presents a well-circumscribed raised plaque composed of small nodules with a scaly, crusted surface having a dull-red color about 2 in. in diameter on the skin of the right knee.

(1) Tuberculin tests: OT 1:1,000,000 and 1:100,000, negative.

(2) X-ray examination reveals "no evidence of a radiopaque foreign body."

(3) Urine examination, negative.

(4) Microscopic examination (Report of Dec. 4, 1957): Section shows an acanthotic epidermis, the upper two-thirds of which are filled with granulation tissue dilated with blood vessels. In the lower one-third of the section are islands of inflammatory exudate, consisting of foreign-body giant cells, as well as occasional Langhans cells. The blood vessels in this area have hypertrophic walls. The cellular exudate consists largely of lymphocytes.

(5) Cultures and guinea pig inoculation for tubercle bacilli have been instituted.

(6) Studies for silica and other foreign material in the microscopic sections are being performed.

Diagnosis: Foreign-body granuloma.

### Discussion

DR. VICTOR H. WITTEN: I just want to ask whether the presence of Langhans cells in the section would suggest a diagnosis of a tuberculoderm rather than a simple foreign-body granuloma. One might very well expect to find evidence of silica in a lesion if it were produced by scraping on sand or on the street.

DR. ARTHUR B. HYMAN: In swimming pool granuloma, which is supposed to be due to an organism that is similar to the tuberculosis organism, there is a histologic picture closely resembling tuberculosis. That was not the picture of this slide, where there was a fairly banal type of foreign-body granuloma. I do not know whether the polarizing microscope was used, but one should look at the slides with polarized light. If there is a foreign body, it would probably be best seen in the giant cells.

DR. CHARLES WOLF: To me it seems that the case could be classified as tuberculoma, in other words, lupus vulgaris. I wish to recall to the Section that a few years back we had the good fortune to have the Swedish or Norwegian author, who gave us a very clear delineation of the condition that occurred in his country where several cases of lupus vulgaris appeared following swimming pool accidents, and I believe this case fits into that group, despite the fact that there are not typical lupus vulgaris nodules of the apple-jelly-colored appearance. I, therefore, would call it tuberculoma or lupus vulgaris type of lesion.

DR. MARION B. SULZBERGER: I think this case should be discussed more fully, especially for the benefit of the younger members of this audience. Dr. Wolf referred to Professor Hellerström, of Sweden, who was here at one of our Section Meetings and discussed the swimming pool injuries and the granulomas which appeared subsequently to these injuries. If I am correct, there is now pretty good agreement that a particular bacillus caused most of these lesions. I believe this bacillus is called Bacillus balnei. I believe that it has also been reported that some rare cases of swimming pool granuloma were due to tubercle bacilli.

Now for the question of the term "foreign-body granulomas." Saying that the lesion is simply a "foreign-body granuloma" seems to me an oversimplification. There are, for example, types of foreign bodies that produce changes which resemble sarcoidosis, especially if the foreign body happens to be a beryllium or a silicon particle. It has been known since the time of J. Jadassohn and Lewandowsky that some micro-organisms and their products produce allergic-like granulomas that are almost indistinguishable from certain types of foreign-body granulomas.

Moreover, there is a good evidence, first in the work of Ervin Epstein and others and later in the work of Shelley, that granulomas from such elements as silicon, beryllium, and zirconium salts

can be based on allergic (immunologic) sensitization mechanisms, analogous to granulomas due to tubercle bacilli, lepra bacilli, fungi, treponemes, etc. We must bear all of these things in mind in discussing such a case with lesions appearing after and at the site of injury.

DR. DOUGLAS P. TORRE: Clinically there seemed to be quite a bit of deep infection. The microscopic slide showed pockets of neutrophils, quite deep under the epidermis. I think the infection here acts as the foreign body, and the granulomatous reaction is due to the chronic infection. More bacteriological studies should be done. Thorough curettement, opening all the sinuses, might effect a cure.

DR. MAURICE J. COSTELLO: I was not aware in this case, on close examination, of any pockets or fistulae as are frequently seen in the swimming pool granulomas. We have a student nurse at one of the hospitals now who has that condition. There are many fistulae and pockets and areas of wandering infection throughout the lesion. We have tried just about everything in the treatment of the condition without the slightest bit of improvement. I did not get the impression that these features were present in the lesion of the patient presented.

Incidentally the girl I referred to developed her lesion when she fell at the seashore, and there was some relationship between the environment and the occurrence of the condition. This boy fell on a sandy path, and he possibly could have a silicon granuloma.

One time in the report by Ervin Epstein of a case of silicon granuloma on the face, the silicon granuloma disappeared under steroid therapy.

I also would like to ask Dr. Nelson how one goes about discovering this organism and proving the condition. During the course of a year we see two or three of these cases.

Our patient still has the condition after extensive conventional treatment.

DR. CARL T. NELSON: Mycobacterium balnei and Mycobacterium ulcerans are acid-fast rods, which characteristically grow best at 31-32 C, not at 37 C. They grow on simple egg media used for other acid-fast rods. There really is no problem in growing these organisms provided the laboratory is told that the specimens should be incubated at 32 C, not at 37 C. In the one case of M. ulcerans seen at Presbyterian Hospital, treatment was, as Dr. Costello points out, very disheartening until the patient's lesion was exposed regularly to a heat lamp. This was done at the suggestion of Miss Balbina Johnson, and the heat lamp in itself was sufficient to do most of the treatment for us. M. ulcerans and M. balnei simply do not thrive at 37 C or higher temperatures.

Norden, who has written a large monograph on M. balnei, the cause of swimming pool granulomas, assures me that M. balnei is not the same organism as the M. ulcerans. I think that this should still be open to discussion. It is very interesting that these organisms are peculiarly pathogenic for rats and mice. If M. balnei is injected intraperitoneally into mice or M. ulcerans intraperitoneally into rats, the animals will develop ulcerations of the paws and distal tail. That is, the parts of the body that are cooler are the areas that develop the ulcers.

DR. JESSE A. TOLMACH: Before I close I would like to ask Dr. Nelson whether infection with M. balnei produces a positive tuberculin reaction.

DR. CARL T. NELSON: We think so. In fact, in the series of cases reported by Zettergren and others, 24 patients were known to have negative tuberculin reactions prior to their infections with M. balnei. All developed positive tuberculin reaction after the appearance of the skin lesions.

DR. JESSE A. TOLMACH: In the six cases Hellerström reported, guinea pig inoculations were negative. In five of the six cases tuberculin tests were negative prior to the eruption and became positive subsequent to the appearance of the skin lesions. It was on the basis of the subsequently developed positive tuberculin reactions and the absence of a tuberculous focus elsewhere that he made the diagnosis of primary-inocluation lupus vulgaris. I believe that in one instance he was able to collect tubercle bacilli in the sediment from a pool which one of his patients used. In view of what Dr. Nelson has told us tonight, it is more likely that M. balnei, rather than the tubercle bacillus, was the responsible organism.

In 1953, Dr. S. B. Frank and I reported a case similar to Hellerström's cases (*J. A. M. A.* 151: 724-726, [Feb. 28] 1953). To answer Dr. Costello's question, in our case, applications of Promin jelly cleared up the lesion, though I must say it might have subsided spontaneously.

The case we are now discussing, however, cannot be a swimming pool granuloma because there was not history of a swimming pool injury. Furthermore, microscopic examination of the tissue revealed a foreign-body granuloma, and polariscopic examination showed the presence of crystals, the nature of which has not yet been determined.

**Idiopathic Multiple Hemorrhagic Sarcomata (Kaposi's Sarcoma).** Presented by DR. FREDERICK REISS.

### Discussion

DR. DAVID BLOOM: This patient was under my observation at Bellevue Hospital for a number of years. He was treated for erythroderma associated with severe pruritus. The biopsy examination revealed, at that time, unspecific dermatitis. A mini-

mum of 40 mg. of Meticorten was necessary to control the severe pruritus. About one year ago a small, erythematous, mildly infiltrated lesion on the trunk appeared which was diagnosed by the pathologist as Kaposi's sarcoma. Recently numerous such lesions appeared on the trunk which again were diagnosed pathologically as Kaposi's sarcoma. If the histopathologic diagnosis is accepted, we are dealing with an unusual history and clinical picture of Kaposi's sarcoma.

DR. ARTHUR B. HYMAN: Sections from two specimens from this patient showed undoubted Kaposi's sarcoma.

DR. ORLANDO CANIZARES: There is a further interesting clinical point. I don't know if Dr. Bloom stressed it enough. This patient had a similar crop of lesions about a year ago which healed spontaneously. At that time the biopsy was suggestive of Kaposi's but not definite. This crop of lesions appeared very recently, and now the histologic diagnosis is more conclusive.

DR. ARTHUR B. HYMAN: The facts that the patient had exfoliative dermatitis before the more typical lesions of Kaposi appeared and that there are blood changes indicating the presence of some kind of blood dyscrasia related to polycythemia vera would fit into the fairly accepted idea today that there is more than a chance relationship between the malignant lymphomas and Kaposi's sarcoma. Polycythemia, in turn, is closely related to and may be associated with the leukemias and other lymphomas.

DR. MAURICE J. COSTELLO: I want to add a note. Dr. Segal and I presented a paper at the last meeting of the American Academy of Dermatology concerning a patient with erythroderma psoriaticum who was on our wards at Bellevue Hospital for two years. This patient developed Kaposi's sarcoma which was proved by biopsy.

**Keratosis Follicularis (Darier's Disease).** Presented by DR. DAVID BLOOM.

**Acute Disseminated Lupus Erythematosus.** Presented by DR. MAURICE J. COSTELLO.

**Leprosy, Lepromatous Type.** Presented by DR. MAURICE J. COSTELLO.

**Sarcoidosis.** Presented by DR. MAURICE J. COSTELLO.

**Favus.** Presented by DR. A. B. HYMAN and DR. N. GOLDFARB (by invitation).

**Micropapular Tuberculid.** Presented by DR. A. B. HYMAN and DR. H. STRAKER (by invitation).

**Scleroderma.** Presented by DR. ARTHUR B. HYMAN and DR. GERALD R. FROLOW (by invitation).

**Case for Diagnosis: Sclerosis of the Skin Associated with Acromegaly.** (Presented in May, 1957). Presented by DR. IRVING MILBERG.

**Case for Diagnosis: Aberrant Mongolian Spot; Ota's Blue Nevus?** Presented by DR. KATE MILLER.

**Extensive Leukoplakia of Mouth.** Presented by DR. HELEN J. NEAVE.

**Lichen Planus.** Presented by DR. FREDERICK REISS and DR. M. COOPER (by invitation).

**Multiple Noduli Cutanei.** Presented by DR. S. ROBBINS and DR. S. KATZ (by invitation).

**Hansen's Disease, Lepromatous Type.** Presented by DR. MABEL G. SILVERBERG.

**A Case of Autograft in Vitiligo.** Presented by DR. GERALD A. SPENCER and DR. JESSE TOLMACH.

**Micropapular Tuberculid.** Presented by DR. BRAITMAN and DR. BERSANI (by invitation).

**Lupis Vulgaris.** Presented by DR. NATHAN SOBEL and DR. ANDREW FRANKS (by invitation).

## PHILADELPHIA DERMATOLOGICAL SOCIETY

**James M. Flood, M.D., Chairman**

**Herbert A. Luscombe, M.D., Secretary**

**Jan. 17, 1958**

**Pyoderma Gangrenosum: Probable Ulcerative Colitis; Pregnancy (Four Months).** Presented by DR. DONALD M. PILLSBURY and (by invitation) DR. L. D. AARONSON.

A white woman aged 25, in moderate distress, complaining of pain in her right leg, presented on the extensor aspects of her elbows and on her buttocks numerous raised, firm, brownish lesions. On the left thigh was a large, circumscribed area of dermatitis measuring 14 cm. in diameter. This area consisted of an inner and an outer zone of granulation tissue separated from each other by a depressed zone 0.5 cm. in width containing purulent material. On the right lower leg was an extensive area of ulceration extending from the lateral aspect of the right ankle and continuing upwards, involving the lower half of the right leg. Distally there appeared to be granulation tissue and new skin. Proximally was a necrotizing border of skin which was grossly infected.

The patient, who was born in Germany but who has been in the United States for the past three years, apparently enjoyed excellent health until the birth of her second child prematurely at eight months, in April, 1957. She is now four months pregnant. Most of her present illness started about one week after the birth of the second child, at which time she developed simultaneously diarrhea and multiple furuncles on her buttocks and in the perineal and pubic areas. The diarrhea consisted of three to four diurnal and four to five nocturnal

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bowel movements. The stools were soft and watery with a fair quantity of mucus and blood specks. She denied any significant weight loss. Furuncles also developed on her left thigh and on the lower third of her right leg. Then lesions progressed to form large abscesses which subsequently coalesced to form deep ulcers. The remaining furuncles resolved, leaving circumscribed keloid-like masses. On Dec. 17, 1957, she was admitted to Metropolitan Hospital, where she remained for 18 days. She was treated for furunculosis and ulcerations on her legs, buttocks, and elbows. Treatment consisted of daily soaks, surgical debridement, application of Chloromycetin cream to the ulcerations, and petrolatum gauze dressings. Beginning Dec. 24, 1957, she was given 100 cc. of serum albumin for three successive days, the albumin-globulin ratio being 1:2. During this hospital stay, the ulcerative areas and furuncles on other parts of the body improved with the exception of the ulcerations on the right ankle and foot, which became progressively worse. She was admitted to the Hospital of the University of Pennsylvania in January, 1958, for further evaluation and treatment.

Examination of the heart revealed tachycardia with a Grade 2 systolic murmur heard at the apex. Abdominal examination revealed the presence of a mass extending two-thirds of the way up to the umbilicus.

A complete blood cell count on Jan. 14, 1958, revealed 8.2 gm. hemoglobin, 5200 leukocytes, 75 neutrophils, 2% monocytes, 23% lymphocytes, 306,000 platelets. The serologic tests for syphilis showed the Kolmer nonreactive, the Kline weakly positive. Urinalysis showed specific gravity 1.016, protein 1+, no sugar, 0 to two erythrocytes per high-power field. Examination of feces on Jan. 16 showed color light brown, consistency soft. Microscopic examination showed many pus cells; guaiac was negative for occult blood. A second specimen showed guaiac slightly positive. On Jan. 10, plasma protein totaled 7.1 gm. per 100 cc., with albumin 2.5 gm. per 100 cc. and globulin 4.6 gm. per 100 cc.; serum calcium was 8.6 mg. per 100 cc. The blood glucose test, two hours postprandial, 88 mg. per 100 cc. The blood urea nitrogen was 8 mg. per 100 cc.; serum bromide level, 25 mg. per 100 cc. On Jan. 25, the hematocrit value was 29. The sedimentation rate was 63 mm. in an hour; corrected, 34 mm. in an hour.

Two strains of coagulase-positive hemolytic Staphylococcus pyogenes var. aureus were isolated from tissue obtained at biopsy. No anaerobes were present. Smear and culture from the ulceration on the left thigh showed (1) diphtheroids; (2) hemolytic S. pyogenes var. aureus (coagulase-positive), sensitive to most of the antibiotics; (3) occasional Pneumococcus; (4) occasional alpha Streptococcus. Smear and culture made from ulceration on the right leg showed Pseudomonas and moderate hemolytic S. pyogenes var. albus (coagulase-positive) sensitive to all antibiotics but penicillin. On Jan. 16 proctoscopic examination was made with the proctoscope passed to 12 cm. and revealed a red, friable mucosa which bled easily. No frank ulcerations were seen.

A roentgenogram of the chest on Jan. 16 showed a pleural reaction at the right base with a moderate elevation of the right diaphragm.

The reports on biopsies were as follows:

Specimen A (from the left thigh): "This specimen showed hyperplastic epidermis and a chronic inflammatory process in the corium. Fibrosis was prominent with loss of appendages and necrosis with foam cells of the subcutaneous fat. In the deeper part of the corium the fat was largely destroyed and many epithelioid cells and giant cells with foamy cytoplasm as well as numerous lymphocytes were present. The upper part of the corium showed intense inflammatory reaction with increased numbers of vessels. Pathologic Diagnosis: Chronic granulomatous inflammation with fibrosis and fat necrosis."

Specimen B (from the right leg): "This specimen showed hyperplastic epidermis with an intense solid inflammatory reaction of the corium. A thin zone of connective tissue separated the epithelium from the granulation tissue composed of polymorphonuclear leukocytes, lymphocytes and edema with large numbers of small vessels. The subcutaneous fat was equally involved and largely replaced by the inflammatory cells. This is suggestive of pyoderma (abscess) at the margin of an ulcer. Pathologic Diagnosis: Abscess (ulcer)."

The patient has been treated with continuous warm saline compresses applied to the ulcerated areas. Surgical debridement has been carried out on several occasions. Erythromycin, 250 mg. q. i. d., has been given. The diet has been high in protein and calories and low in residue, with supplementary vitamins. On Jan. 16 she received 500 cc. of whole blood. On Jan. 11 she received 10 cc. of γ-globulin intramuscularly. Codeine, 0.033 gm. (½ grain), and acetylsalicylic acid have been given to control pain.

## Discussion

DR. THOMAS BUTTERWORTH, Reading: I have had fairly good results in these cases with Azulfidine, which has been recommended by Dr. Louis Brunsting. I find very few patients can tolerate the recommended two 0.5 gm. tablets every three hours around the clock, but I have had very good results with smaller doses.

DR. GEORGE B. HAMBRICK: What is the consensus about extensive surgical debridement in such a case?

DR. JOHN P. SCULLY, Reading: Should there not be more of a supportive treatment rather than surgical treatment, proceeding with doses of γ-globulin, steroids and high protein intake? Has she an ulcer?

DR. L. D. AARONSON (by invitation): This woman was proctoscoped yesterday morning, and they had a little difficulty passing the proctoscope because of her pregnancy. They did see some friable mucosa but no definite ulcer.

DR. M. H. SAMITZ: Treatment depends upon the causation of these lesions. The lesions, as far as I could make out in studying six cases, may arise first as a result of transportation of organisms from the colon itself to other areas of the body, with ulcerations of the infected skin sites. Second, the mechanism in the production of these lesions is usually that of a Shwartzman phenomenon. The third probability is a specific type of sensitivity, giving the picture of a necrotizing angiitis. The ulcerated lesions may be produced by any one of these mechanisms, or by a combination of the three. However, in association with these mechanisms is a primary nutritional defect, and in the treatment of these patients, the most important thing is the correction of the colon disease. Stool cultures should be done to determine whether or not the same bacterial flora is present in the skin lesions. In two cases we followed, we found colon bacilli in the skin lesions identical with those found in the stools. Such studies allow for the use of the proper antibiotic or chemotherapeutic drug. If we consider the possibility of a Schwartzman reaction, or a specific type of sensitivity, we may consider the use of steroids. However, one must be careful about steroids and be certain that the colonic ulcerations show no evidence of perforation. I believe γ-globulin is an excellent adjuvant to fortify the antibody response. Local therapy of the skin lesions requires a simple cleansing routine and bed rest. A high-protein, nonroughage diet supplemented by vitamins is, of course, essential.

DR. JOHN P. SCULLY, Reading: Does Dr. Pillsbury think the finding of colon bacilli would have any more significance than the finding of a yeast organism, such as Candida?

DR. ALBERT M. KLIGMAN: I think this lesion is a phagedenic ulcer which has developed in a person of very low resistance. It is simply a secondary bacterial infection. Many kinds of organisms may participate.

DR. DONALD M. PILLSBURY: This patient is obviously sick, and looking at her without knowing her history, you could think she has ulcerative colitis. There is obviously some serious systemic disease present.

DR. LOUIS JAFFE, Pottstown: Has it been established that the colitis is ulcerative colitis?

DR. L. D. AARONSON (by invitation): We are awaiting further studies on the stool cultures, and so on. It has not been definitely established that this is ulcerative colitis.

DR. L. J. SCHAMBERG: This woman is quite similar to a patient of Dr. Milton Cahn, except that his patient was in good health but for a severe phagedenic ulcer of the calf. I should like to ask Dr. Kligman if most of these patients are systemically ill.

DR. ALBERT M. KLIGMAN: They are not usually in good health. Often you can locate a primary etiologic factor. Not every case has ulcerative colitis, however.

**Erythema Nodosum Following Steroid Withdrawal; Rheumatic Fever (?), Inactive.** Presented by DR. DONALD M. PILLSBURY and (by invitation) DR. SIDNEY GROSS.

A Negro boy aged 10, obese, with moon face and increased facial and body hair, when first seen on Jan. 10, 1958, presented tender, erythematous, subcutaneous nodules 1 to 5 cm. in diameter distributed symmetrically over the extensor surfaces of the arms and legs and on the cheeks. During the past week the erythema has subsided and the tenderness and induration of the lesions have diminished. There were moderately firm axillary and inguinal nodes. In 1948, the patient was treated at the Philadelphia General Hospital for meningitis. In June, 1956, he had acute rheumatic fever with chorea and carditis, for which he was hospitalized at the Hospital of the University of Pennsylvania. In April, 1957, he again entered the university hospital with an acute exacerbation of rheumatic fever, which was treated with penicillin and cortisone, 400 mg. daily, gradually reduced over the next four months. He was transferred to the Children's Seashore House in Sept., 1957. He was maintained on prednisone, 5 mg. t. i. d., and penicillin, 200,000 units per os daily. On Dec. 17, 1957, prednisone was stopped and respository corticotropin injection (ACTH gel) was given for the next four days. On Dec. 28, 1957, the patient had a fever with temperature of 102 F; then he was afebrile until Jan. 5, 1958, when he developed painful, erythematous, subcutaneous nodules on the extensor surfaces of both arms and legs as well as the cheeks. His fever recurred at that time, and he was referred back to the university hospital.

Medical examination showed the chest clear to auscultation with no heart thrills or murmurs and no abdominal organs palpable.

A complete blood cell count taken on Jan. 9, 1958, revealed 12.6 gm. hemoglobin, 19,800 leukocytes, 69% neutrophils, 2% eosinophils, 3% monocytes, 36% lymphocytes. On Jan. 15, 1958, the count showed 11.6 gm. hemoglobin, 8800 leukocytes, 68% neutrophils, 3% eosinophils, 6% monocytes, 23% lymphocytes. The corrected sedimentation rate

was 33 mm. in an hour. Urinalysis showed a trace of albumin but was otherwise within normal limits. Plasma protein was 6.7 gm.; albumin, 4.0 gm.; globulin, 2.7 gm. C-reactive protein, 6+; antistreptolysin titer, 60 Todd units. Test with purified protein derivative No. 1 was negative. A roentgenogram of the chest on Jan. 10, 1958, showed heart and lungs to be normal. An electrocardiogram gave a normal tracing except for tachycardia.

The report on the biopsy specimen was as follows: "January 4, 1958, #18862: This specimen of skin showed a moderately wavy epidermis with hyperkeratosis, keratotic plugging and mild acanthosis. The dermis was essentially normal but the hypoderm showed numerous small scattered aggregates of foam cells intermixed with a few lymphocytes and an occasional eosinophil. Occasionally large foci of foamy foreign body giant cells, epithelioid, lymphocytes and foam cells were seen arranged in a haphazard pattern. Little or no involvement of the blood vessels, or caseation, was present. Diagnosis: Panniculitis."

The patient has been treated with 200,000 units of orally administered penicillin daily as prophylaxis.

### Discussion

DR. JOHN E. GERMAN, Reading: This boy, I think, certainly has activity of his rheumatic state. The C-reactive protein is 6+ and his antistreptolysin titer is 60, which is an indication of a great deal of activity of his rheumatic state. I rather think these lesions are due to rheumatic activity.

DR. MARGARET GRAY WOOD: The histologic picture is that of panniculitis. A recent report in the literature was brought to my attention by Dr. Gross and Dr. Hambrick in which, following the withdrawal of steroid therapy, an erythema nodosum-like picture developed which was histologically a panniculitis with necrotizing vasculitis. A similar picture is presented by this patient.

DR. HERMAN BEERMAN: It is not erythema nodosum histologically; rather, it is panniculitis. I have no idea as to the cause.

DR. SIDNEY GROSS (by invitation): Smith, Good, and Zak (*A. M. A. J. Dis. Child.* 93:77 [1957]) reported 11 cases in which high doses of steroid were used, and 5 of the 11 patients developed lesions on the elbow, pruritic, tender nodules on the extensor surfaces, after steroid withdrawal. They did not have increase in antistreptolysin titer; 50 to 150 units is borderline activity in this hospital. These lesions subsided in these five cases in 4 to 14 days. This child has had lesions for about two weeks, and they have subsided. These 11 patients had rheumatic fever but had no recurrence at this time. The Pediatrics Department here does not feel that this patient has active rheumatic fever.

**Bromoderma.** Presented by DR. DONALD M. PILLSBURY and (by invitation) DR. L. D. AARONSON.

**Darier's Disease.** Presented by DR. DONALD M. PILLSBURY and (by invitation) DR. L. D. AARONSON.

**Parapsoriasis, Guttate Type.** Presented by DR. DONALD M. PILLSBURY and (by invitation) DR. C. G. MENDELSON.

**Case for Diagnosis (Probable Tuberculosis Verrucosa Cutis; Diabetes Mellitus; Bilateral Cataracts; Bilateral Deafness, Cause Undetermined; Latent Syphilis, Adequately Treated).** Presented by DR. DONALD M. PILLSBURY and (by invitation) DR. SIDNEY GROSS.

**Case for Diagnosis: Nevus; Juvenile Flat Warts; Xanthoma?** Presented by DR. MARGARET GERLACH MAHONEY for diagnostic and therapeutic suggestions.

**Alopecia Totalis.** Presented by DR. WALTER B. SHELLEY and (by invitation) DR. J. S. HARUN to demonstrate the effects of Triamcinolone.

**Psoriasis.** Presented by DR. DONALD M. PILLSBURY, DR. WALTER B. SHELLEY and (by invitation) DR. J. S. HARUN to demonstrate the effects of Triamcinolone.

**Pityriasis Lichenoides et Varioliformis Acuta (Mucha-Habermann's Disease).** Presented by DR. DONALD M. PILLSBURY and (by invitation) DR. L. D. AARONSON.

**Hypertrophic Scar Beneath a Plastic Surgical Repair of Skin on Bridge of Nose.** Presented by DR. ISADORE ZUGERMAN.

**Pigmented Nevus of Left Cheek.** Presented by DR. JOHN P. SCULLY (Reading)

**Parapsoriasis en Plaques.** Presented by DR. JOHN P. SCULLY (Reading)

**Extensive Nevoxanthoendothelioma.** Presented by DR. MARGARET GRAY WOOD.

**Bowen's Disease (Intraepidermal Epithelioma).** Presented by DR. DONALD M. PILLSBURY and (by invitation) DR. C. G. MENDELSON.

**Sarcoidosis with Involvement of Muscle Simulating Pseudohypertrophic Muscular Dystrophy.** Presented by DR. DONALD M. PILLSBURY and (by invitation) DR. SIDNEY GROSS.

## SAN FRANCISCO DERMATOLOGICAL SOCIETY

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**Jan. 17, 1958**

**Case for Diagnosis: Zirconium Granuloma; Sarcoidosis?** Presented by CAPT. GEORGE B. SKIPWORTH (MC), (U. S. Army) (by invitation).

In March, 1956, this 50-year-old woman was treated for Rhus dermatitis of the face, chest, and arms with a proprietary lotion containing hydrous zirconium oxide and orally administered steroids. A recurrence in July, 1956, was controlled with orally administered steroids and tripelennamine-zirconium cream. An eruption has persisted on her forearms and neck since that time. Subsequent recurrences of a vesicular eruption, presumed to be from poison oak, have been treated with the above medications. The general health has remained good.

There is a dusky-yellow papular eruption on the dorsa of both forearms and similar lesions scattered over the anterior neck. The remainder of the physical examination is negative.

Pertinent blood and urine tests are normal, as are x-ray films of the chest and hands. Tuberculin, coccidioidin, and histoplasmin skin tests are negative. There is a sarcoid-like granulomatous reaction in the tissue removed at biopsy. Special stains for acid-fast bacilli, lepra bacilli, and fungi are negative. There was no reaction to patch tests with the zirconium-containing lotion and cream.

### Discussion

DR. EDWARD J. RINGROSE: The histopathological picture is that of lupus miliaris disseminatus faciei. I believe that this is the same disease process but located on the forearms.

DR. PAUL FASAL: I believe that this is a sarcoid-like reaction to zirconium. It is exactly the picture seen in granulomas of the axilla after the use of deodorant sticks containing zirconium. It resembles tuberculosis and tuberculids very much, but I do not believe that in this instance it is related to tuberculosis.

DR. FREDERICK G. NOVY JR.: I have had the opportunity to see much of this patient. She literally lives in a patch of poison oak. A short time ago she brought in 8 or 10 tubes of ointment, all containing zirconium. She has used these preparations not just once or twice but many, many times. I think that we are dealing with a sarcoid-like reaction to zirconium.

Received for publication Feb. 27, 1958.

DR. REES B. REES: I think that this is a fascinating case. Since hearing Dr. Shelley's wonderful lecture on zirconium granulomas, I have confidently expected a situation of this sort to show up. The next step would appear to be the performance of a skin test with a zirconium salt to see if that would reproduce a lesion.

DR. PATRICK G. BUTLER: This may be a zirconium sarcoid reaction. However, I should like to see this patient have a skin test performed with Rhus antigen. Perhaps she might develop a sarcoid reaction from such a substance, for she told me that her lesions became persistent after an injection of Aquatox. A patient of mine developed lesions at the site of her Rhus dermatitis after such an injection. This condition has persisted for 18 months and necessitates steroids for relief. Histopathologic reports suggest erythema multiforme or possible lymphoma. It may be possible for a sarcoid reaction to occur under similar circumstances.

DR. GEORGE B. SKIPWORTH: Since the spring of 1956, cases have been reported of granulomas occurring in the axillas following the use of stick deodorants, most of which contained a salt of zirconium. It is surprising that no cases have been reported of granulomas occurring in other sites, particularly since zirconium products are used widely for treatment of poison oak dermatitis. Skin tests were performed on this patient, with use of both the lotion and ointment over abraded surfaces, with no reaction after 48 hours. These sites will be rechecked in three weeks. Polaroscopic and spectrographic analysis results are pending.

**Dermatomyositis.** Presented by DR. WALTER E. WEBER.

A 64-year-old man was first examined in June, 1955, because of erythema and puffiness of the light-exposed areas and mild weakness of three months' duration. Now there is diffuse erythema of the face, neck, and forearms and difficulty in swallowing.

The course has been stormy. He lost weight, going from 170 to 80 lb., but has gained again to 120 lb. There have been long periods of hospitalization and rehabilitation. Bronchopneumonia, mental depression, pyoderma, regurgitation of food, and inability to swallow have complicated the disease. There have been severe exacerbations of dermatomyositis so that he was on the critical list during hospitalization. He has improved gradually

for the past year, during which he has not been hospitalized.

There has been an increased excretion of creatine. Otherwise the extensive laboratory tests have been essentially normal.

Only steroids gave any appreciable benefit during the acute exacerbations. No specific medication has been used during the past three months. Corticotropin (ACTH), prednisolone, testosterone, α-tocopherols, amino acid concentrates, vitamins, antibiotics for pneumonia, topical therapy for pruritus and pyoderma, and physical therapy have been prescribed.

### Discussion

DR. MARION B. SULZBERGER (by invitation): The case clinically, the description of the course, and the findings on the biopsy are all characteristic. The questions I have in my mind are as follows: How many of these cases are found to have visceral malignant tumors? And how many of these are relieved when the tumors are removed when they are operable? Is the occurrence of the dermatosis and of such tumors of the same incidence in males as in females?

DR. ERVIN EPSTEIN: The incidence of visceral tumors in dermatomyositis is about 6%. This is identical with the incidence in similar age groups without dermatomyositis.

DR. EDWARD W. WILSON: We have just reviewed 22 cases of dermatomyositis which were seen over the last 10 years at Stanford. There was no history or evidence of malignancy in any of them.

DR. WALTER E. WEBER: It appears that the incidence of malignancies with dermatomyositis is insufficient for statistical validity. There does not appear to be any increase in malignancies in children with this disease. Therapy of dermatomyositis requires the combined efforts of the dermatologist, internist, and physical therapist. Steroids are life saving during the crises and are the main factor in the survival of the patient presented. I have not been impressed with the effect of testosterone.

**A Case for Diagnosis: Poikiloderma Vasculare Atrophicans; Early Mycosis Fungoides?** Presented by DR. JAMES P. MCGINLEY.

A 43-year-old man has had an eruption on the face, arms, and legs for eight months. There are large patches of reticulated telangiectasia with scaling, and some atrophic areas followed what the patient described as "poison oak rash." There is a subsiding pyoderma on the right side of the face.

### Discussion

DR. MERLIN T. R. MAYNARD: It is easy to confuse premycotic mycosis fungoides with psoriasis. A patient of mine with clinical and histological psoriasis slowly developed mycosis fungoides over a period of about 25 years and died only last year.

DR. MORTIMER S. FALK: One of my patients with mycosis fungoides became resistant to x-ray therapy after responding well to an initial course. I then treated her with 100 r daily for 10 days instead of the conventional method at weekly intervals. She again responded to the radiation. I think that this is logical. We do not treat epitheliomas at weekly intervals, as we know that a greater total dosage would be required. It is reasonable to expect that radioresistant treated cases may respond to repeated doses at closer intervals.

DR. KEMP H. DOWDY: I have used antimony potassium tartrate (tartar emetic) in a limited number of cases. It helps some but fails in others. The intramuscular route, which is painful, seems to work better than the intravenous route.

DR. MARION B. SULZBERGER (by invitation): I should like to speak about this case. This patient has a picture which in Europe they used to call parakeratosis variegata, and that would fit both of these diagnoses. This case has the characteristics of both parapsoriasis or premycotic parapsoriasis and poikiloderma vasculare; clinically, this certainly conforms to the diagnosis of parakeratosis variegata.

Now about therapy: The work of John Garb with antimony potassium tartrate is fascinating. I saw his first cases, particularly the very first one he treated at the Skin and Cancer Unit. This woman's mycosis fungoides just melted away after a few injections of antimony potassium tartrate. Then he had a few more cases that did not respond quite as spectacularly but still improved and did fairly well, with the eventual disappearance of the lesions with just antimony potassium tartrate after other things had failed. But this is another instance of a common phenomenon: To get cured by a drug, hurry and get treated with it as one of the first cases, because later on it may not work. This is what happened with antimony potassium tartrate. I suppose that the psychosomaticists will now say that mycosis fungoides is of psychic origin, because it responded at first and later did not. These are inexplicable phenomena—mysterious. I think that antimony potassium tartrate now is of little value in most cases of mycosis fungoides. The same thing has happened to treatment with sodium *p*-aminobenzoate and vitamins. The only agents I know that help mycosis fungoides are antimetabolites—either radiomimetic drugs or radiation. There are some newer kinds of radia-

tion that can be used. One of them is the teleroentgen procedure introduced by Georg Shirren of Zurich and Munich. With this the patient is placed quite a distance away from a beam of ordinary x-ray, and a beryllium-windowed machine at high milliamperage is used. The patient is sprayed with very superficial rays. The whole body is irradiated, the front with one treatment and the back with another, with the external genitalia protected in the case of a man. Patients with mycosis fungoides or generalized erythrodermas who have not responded to other x-ray sometimes still respond to large doses of this type of nonpenetrating rays. Another treatment is the one that is being carried out by Dr. Fromer at the Lahey Clinic and Dr. Van Scott at the National Institutes of Health with $\beta$-rays—the electron beam. This requires big and expensive machines in contrast to the machines used in the teleroentgen treatment. We recently had a case that was moribund and no longer responded to any kind of x-ray (including the teleroentgen treatment). We sent her to Fromer, and she has had another excellent remission after being treated with the electron beam.

DR. WILLIAM F. B. HARDING: I also am impressed by the long duration of this man's eruption, realizing that over the 20-year period it did not always look as it does now. He has remained unusually well in every respect and continues to work in an outdoor job daily. I am reluctant to initiate any therapy which might disable him unless the condition deteriorates to the point where that must be done.

**Raynaud's Phenomenon; Scalenus Anticus Syndrome?** Presented by DR. RODERICK D. SAGE (by invitation) and DR. EUGENE M. FARBER.

**Case for Diagnosis: Sarcoidosis; Tuberculid?** Presented by DR. GEORGE T. LENAHAN.

**Embryonal Fibrolipoma.** Presented by DR. EDWARD J. RINGROSE.

**Granulomatosis Disciformis Chronica et Progressiva.** Re-presented by DR. ERVIN EPSTEIN.

**Cutis Laxa.** Presented by DR. JAMES P. MCGINLEY.

**Case for Diagnosis: Psoriasis with Contact Dermatitis?** Presented by DR. HERBERT L. JOSEPH.

**Lichen Pilaris seu Spinulosis.** Presented by DR. ERVIN EPSTEIN.

**Congenital Lymphedema of Extremities and Face.** Represented by DR. MANUEL F. ALLENDE and DR. MICHAEL J. FRANZBLAU (by invitation).

**Case for Diagnosis: Pathergic Granulomatosis; Wegener's Granuloma?** Presented by DR. JOHN H. EPSTEIN and DR. JOHN V. WHEELESS (by invitation).

**Lymphoma; Mycosis Fungoides?** Presented by DR. WALTER E. WEBER.

**Mycosis Fungoides.** Presented by DR. WILLIAM F. B. HARDING.

# Abstracts from Current Literature

TWENTY-ONE YEARS' EXPERIENCE WITH REJECTIONS FOR EMPLOYMENT. A. F. MANGELSDORFF, A. M. A. Arch. Indust. Health 17:104 (Feb.) 1958.

Over a 21-year period, 36,888 applicants were examined for employment in a large chemical company. Of this group, 8.56% were rejected for employment on a medical basis and 7.42%, because of dermatitis. During the first 10 years 4.71% were rejected because of dermatitis; in the last 11 years, 12.48% were rejected for this reason. In this last period, dermatitis ranked fourth among the causes for rejection, after cardiovascular diseases, chest x-ray abnormalities, and abnormal urine findings. The author, in speculating about the causes for the recent increased importance of dermatitis in employment rejection, wonders whether more persons are becoming sensitive to the environment, perhaps from the use of detergents, or whether examiners exercise more care to avoid possible compensation action.

NORINS, Chicago.

HIRSUTISM. W. H. PERLOFF, H. E. HADD, B. J. CHANNICK, and J. H. NODINE, A. M. A. Arch. Int. Med. 100:981 (Dec.) 1957.

In a group of women with idiopathic hirsutism, the authors found the urinary levels of total 17-ketosteroids and the $C_{19}O_3$ fractions (weak androgens) to be generally higher than in a control group of patients, although there was some overlapping of values. They did find, however, the $C_{19}O_2$ 17-ketosteriod fraction (strong androgens) to be uniformly elevated, and the level was reduced by giving 7.5 to 15.0 mg. of prednisone daily. During the course of treatment, they found reduction in the amount, rate of growth, and coarseness of superfluous hair, particularly when wax depilation was performed concurrently. Significant results occurred within three to eight months.

NORINS, Chicago.

MALIGNANT CARCINOID TUMOR: ALTERED REACTIVITY OF THE SKIN TO SEROTONIN IN TWO PATIENTS. M. ROTBART, California Med. 88:112-113 (Feb.) 1958.

Appropriately controlled tests were carried out in two cases of patients with carcinoid tumors and abnormal circulating levels of serotonin to verify a hypothesis that such patients would have a greater tolerance for exogenous serotonin than would normal persons. Contrary to the hypothesis, the patients had not less but more reaction to intradermal injection of serotonin than to histamine and also more reaction than normal persons.

If this altered reactivity were to be observed consistently in large series of patients with malignant carcinoid disease, it might be used as a presumptive test.

ALLENDE, San Francisco.

OBSERVATIONS ON HYPOPARATHYROIDISM: I. EXFOLIATIVE DERMATITIS AS THE PRESENTING SIGN OF HYPOPARATHYROIDISM: A CASE REPORT. A. HARELL-STEINBERG et al., J. Clin. Endocrinol. 17:1095 (Sept.) 1957.

A 35-year-old woman developed exfoliative dermatitis as a presenting sign of hypoparathyroidism. The skin cleared, as did the symptoms of hypoparathyroidism, with dihydrotachysterol (AT-10) and vitamin D therapy. There was an exacerbation of symptoms, including the dermatitis, when therapy was suspended. The dermatitis did not respond to corticotropin (ACTH) therapy.

NORINS, Chicago.

FETAL SKIN HOMOGRAFTS. HAMILTON BAXTER and MARCY A. GOLDSTEIN, Transpl. Bull. 5: 26-27 (Jan.) 1958.

Skin grafts from human fetuses between 17 and 38 weeks' gestation were applied to sites of third-degree burns. Eighteen full-thickness fetal skin homografts were applied to six male and two female recipients, aged 1 to 70 years. All of the grafts were rejected in 4 to 46 days, and this was not influenced by the age of the fetus or the sex of either donor or recipient. Since the fetal skin from dogs of younger gestational age does produce less homograft reaction

than that from older dog fetuses, it was suggested that the loss of the younger human fetal skin homografts might be explained by lower resistance to physical trauma. It was concluded that skin grafts from human fetuses between 17 and 38 weeks' gestation do not survive permanently and are not clinically useful for resurfacing granulating wounds.

SMITH Jr., Miami, Fla.

RETICULOSARCOMATOSES OF THE SKIN. G. K. STEIGLEDER and H. G. HUNSCHA, Arch. klin. u. exper. Dermat. 205:435-464 (Feb.) 1958.

Reticulosarcomatoses of the skin are, according to Gans and Steigleder, characterized by an increase of not obviously differentiated connective-tissue cells which therefore are often described as juvenile cells. There are no primary disturbances of the metabolism. Clinically there may be variations from flat, scaly lesions to erythroderma and poikiloderma, from numerous papules to multiple tumors. Although the skin lesions may temporarily improve, the final outcome is fatal. The American definition of these cases as lymphoma is not used by the authors, since the relation of the tissue elements in question to lymphatic tissue has not been proven in all cases. Three instructive tables show the characteristics of cell types described by various authors, give the various names for corresponding cell types, and compare the various histologic descriptions. A fourth table describes the clinical picture and histology of 13 cases of the authors' own material. The authors state that the older names, such as primary multiple sarcomas of the skin, lymphadenosis cutis, and lymphosarcoma, which Gans used in the first edition of his histology text, are sufficient for the characterization of reticulosarcomatoses of the skin.

HOLLANDER, Springfield, Mass.

EXTRACELLULAR CHOLESTEROSIS (KERL-URBACH): A VARIANT OF ERYTHEMA ELEVATUM DIUTINUM. J. J. HERZBERG, Arch. klin. u. exper. Dermat. 205:477-496 (Feb.) 1958.

After thorough histologic study of three cases of extracellular cholesterosis the authors believe that this condition represents a variant of erythema elevatum diutinum. Deposits of extracellular lipids are considered secondary symptoms without nosologic importance. Erythema elevatum diutinum may have a relationship to the nodular allergides of the French school.

HOLLANDER, Springfield, Mass.

RARE FORMS OF TROPHONEUROTIC ULCERS AND THEIR DIFFERENTIAL DIAGNOSIS. R. SCHMITZ, Arch. klin. u. exper. Dermat. 205:497-511 (Feb.) 1958.

Description of a case of ulcerating acropathy of the toes with large painful ulcerations of the calf of the legs in a woman, born in 1894, is presented. This condition is a form of neurovascular dystrophy, seen usually in males and sporadically in females. Pathologic anatomy shows degenerative changes of the spinal ganglia, posterior roots, and columns. Differential diagnostic considerations include pes equinus, malum perforans, trophoneurotic ulcer of the ala nasi, and ulcus cruris postpoliomyeliticum. The first changes of the toes developed in 1911, and the ulceration of the legs, in 1947.

HOLLANDER, Springfield, Mass.

HEPARIN THERAPY AND CLINICAL ASPECTS OF IDIOPATHIC HYPERLIPEMIC XANTHOMATOSIS. R. HAENSCH, Arch. klin. u. exper. Dermat. 205:512-525 (Feb.) 1958.

Injections of depot heparin over a period of several months made xanthomatous lesions subside in two cases. In one case persistent hypertension was reduced to normal level.

HOLLANDER, Springfield, Mass.

ASYMMETRY OF FINGER LENGTHS—A SYMPTOM OF CONGENITAL SYPHILIS? H. D. RÖSLER, Arch. klin. u. exper. Dermat. 205:526-529 (Feb.) 1958.

Asymmetry of finger lengths, which Spiethoff considered a syphilitic stigma, is, according to the author's examinations of 5029 persons, not specific for congenital syphilis.

HOLLANDER, Springfield, Mass.

CIRCUMSCRIBED HYPERHYDROSIS IN FIRST THORACIC SEGMENT CAUSED BY SYMPATHICUS DAMAGE. J. FINKE and H. J. SCHUPPENER, Arch. klin. u. exper. Dermat. 205:530-540 (Feb.) 1958.

Two juvenile patients showed hyperhydrosis in the first thoracic segment, Horner's syndrome, and cervical ribs. The last were most probably responsible for the sympathicus

damage. Deep x-ray therapy of the cervical sympathicus reduced the hyperhydrosis considerably. The authors question whether the triad of symptoms is a constant symptom group which may be observed occasionally.

HOLLANDER, Springfield, Mass.

DIFFERENTIAL DIAGNOSIS OF CANDIDA. HANS RIETH, Arch. klin. u. exper. Dermat. 205:541-550, 1958.

Author presents four tables for easy identification of the various species of Candida. His differentiation of 30 species of Candida and 6 variations is based on the system of the Dutch workers Lodder and Kreger-van Rij. Fermentation and assimilation of dextrose, galactose, saccharose, maltose, and lactose are used for the differentation of Candida species.

HOLLANDER, Springfield, Mass.

CHANGES OF COMPOSITION OF URINE PROTEIN IN CUTANEOUS DISORDERS WITH NEGATIVE URINARY SULFOSALICYLIC ACID TEST. A. KNAPP, Arch. klin. u exper. Dermat. 205:551-561, 1958.

A special method is reported by which normal persons' urine with low protein content could be examined electrophoretically. One distinctly separable albumin and three less distinctly separable globulin fractions were demonstrated. Proteinuria was found in one patient with Sjögren's syndrome, one with xeroderma pigmentosum, and three with pemphigus vulgaris, although there was no evidence of kidney disease and the sulfosalicylic acid test was negative.

HOLLANDER, Springfield, Mass.

ENDEMIC TINEA IN GUINEA PIGS. H. KOCH and H. RIETH, Arch. klin. u. exper. Dermat. 205: 557-585, 1958.

Clinical and mycologic examinations of about 1170 guinea pigs in seven different institutions in Hamburg (no mycologic laboratories were included) showed the existence of tinea. Only one species was found among the animals of the same institution. Trichophyton mentagrophytes and T. rubrum caused these endemic infections. The findings are important, since guinea pigs with endemic tinea represent a source of occupational infection for persons having contact with them. Such infected guinea pigs cannot be used for mycologic experiments.

HOLLANDER, Springfield, Mass.

NEWER EXAMINATIONS ABOUT pH AND ALKALI NEUTRALIZATION OF HUMAN SKIN. H. TRONNIER and H. BUSSIUS, Arch. klin. u. exper. Dermat. 205:586-596, 1958.

A modification of the alkali-neutralization test of the skin is described and compared with Burckhardt's method.

HOLLANDER, Springfield, Mass.

PULMONARY FUNCTION IN ENDOGENOUS ECZEMA. E. LUTZ and G. W. KORTING, Arch. klin. u. exper. Dermat. 205:597-604, 1958.

Various pulmonary-function tests before and after inhalation of an asthmalyticum (Aludrine) were done in 25 patients with endogenous eczema and 20 patients with various dermatoses. All patients were of the same age group. Average age was 24.2 years. Latent asthma disposition (pulmonary dystonia) was found in 60% of eczema patients and in 5% of other patients. No pulmonary dystonia existed in 8 of 12 patients with endogenous eczema in whom there was no personal or familial disposition for asthma.

HOLLANDER, Springfield, Mass.

COLLAGEN AND RETICULO-HISTIOCYTIC TISSUE IN KRAUROSIS PENIS. H. FISCHER and W. NIKOLOWSKI, Arch. klin. u. exper. Dermat. 205:605-616, 1958.

Histologic examination of the prepuce of 11 patients with spontaneous, postoperative, and postinflammatory kraurosis penis. The sclerotic collagenous tissue showed cells with halo formation resembling cartilage cells. There was band-like disappearance of elastic tissue and of perivascular elastic tissue. An infiltrate of round, plasma, and mast cells was found in the border zone between areas abundant in and those poor in elastic tissue.

HOLLANDER, Springfield, Mass.

SKIN AND CERVICAL GLAND TUBERCULOSIS IN EIGHTY-EIGHT TWINS. F. EHRINF and H. NIERMANN, Arch. klin. u. exper. Dermat. 205:617-627, 1958.

Examination of 88 twins with skin and cervical gland tuberculosis proved that the localization of tuberculosis is not influenced by hereditary factors.

HOLLANDER, Springfield, Mass.

ANIMAL EXPERIMENTS ON EPITHELIOID CELL FORMATION IN NORMAL AND TUBERCULOUS ORGANISMS WITH SPECIAL CONSIDERATIONS OF TUBERCULIN SENSITIVITY. H. R. GERBER, Arch. klin. u. exper. Dermat. 205:628-645, 1958.

Intracutaneous and intratesticular injections of dead BCG bacilli and tuberculophosphatid caused epithelioid-cell infiltrates in both normal and BCG infected guinea pigs. Some of these infiltrates showed giant cells. The formation of epitheloid cells developed faster and was more extensive in guinea pigs infected with BCG than in normal guinea pigs. Tuberculin sensitivity was not responsible for quantitative differences of epithelioid-cell formation in normal and tuberculous animals.

HOLLANDER, Springfield, Mass.

EPIDEMIOLOGICAL ASPECTS OF NONVENEREAL "ENDEMIC" SYPHILIS. T. GUTHE and A. LUGER, Dermatologica 115:248-272 (Sept.) 1957.

The present knowledge of nonvenereal syphilis is reviewed on the basis of recent experiences in underdeveloped communities of Bechuanaland, Bosnia, Iraq, Syria, and other areas where "endemic" syphilis has been a health problem. Some 25% to 65% of the people in these areas have been found reactive to serological tests for treponematosis with use of cardiolipin-lecithin antigens. Living habits in underdeveloped areas have established an ecologic balance between host and treponeme. Transmission has been facilitated, the commonest "vector" being the contaminated hands of children. Infection at an early age, rarity of congenital and neurovisceral manifestations, superinfection of latent cases, and reinfection of possibly cured ones are part of this pattern. When the ecologic balance is upset through improvement of environmental conditions, the disease changes its epidemiological, immunological, and clinical pattern to that known in countries where venereal transmission is the rule.

PINKUS, Monroe, Mich.

THE "THERAPEUTIC" EFFECT OF HYDROCORTISONE OINTMENT AND COAL TAR ON EXPERIMENTALLY PRODUCED ECZEMATOUS REACTIONS. H. HAXTHAUSEN, Dermatologica 115: 272-276 (Sept.) 1957.

Four symmetrical sites of contact dermatitis were produced in susceptible persons by application of patch tests. One site served as control. The others were treated with either an oil-in-water emulsion base or with this base containing 1% hydrocortisone or coal tar. No significant therapeutic effects were noted.

PINKUS, Monroe, Mich.

CHEMICAL ASPECTS OF TURPENTINE ECZEMA. S. HELLERSTRÖM, N. THYRESSON, and G. WIDMARK, Dermatologica 115:277-286 (Sept.) 1957.

Freshly distilled Swedish turpentine does not cause skin reactions in sensitive persons, but slight oxidation produces compounds of high reactivity. Of the four major constituents of turpentine ($\Delta^3$-carene, $\alpha$-pinene, $\beta$-pinene, limonene), $\Delta^3$-carne seems to be the source of most of the sensitizing oxidation products.

PINKUS, Monroe, Mich.

EXPERIENCES IN PENICILLIN TREATMENT OF ENDEMIC SYPHILIS IN SERBIA. S. ILIC, Dermatologica 115:287-293 (Sept.) 1957.

Administration of from 3,600,000 to 6,000,000 units of procaine penicillin in oil with aluminum monostearate to patients in two districts of relatively fresh endemic syphilis produced seronegativity in 63% to 71% of the cases. In three other districts in which syphilis had been endemic for a long time, 38%, 38%, and 60% seronegative results were recorded 18 months after treatment. Eighty per cent of all the patients treated had syphilis in the latent stage.

PINKUS, Monroe, Mich.

A Case of Nevus Sudoriparus with Hyperhidrosis. S. Lapière, Dermatologica 115:293-297 (Sept.) 1957.

A 51-year-old woman presented a slightly pigmented and erythematous plaque on the right side of the neck which constantly produced an increased amount of sweat. Histologic examination showed hypertrophic eccrine sweat coils forming an almost continuous layer in the deep portions of the cutis.

Pinkus, Monroe, Mich.

Statistical Control of a Laboratory Method: Distribution and Frequency of Anticomplementary Action in the Bordet-Wassermann Test. A. Linder and R. Brun, Dermatologica 115:298-303 (Sept.) 1957.

A statistical analysis of more than 100,000 tests showed that anticomplementary sera were distributed at random and that no technical factor could be incriminated.

Pinkus, Monroe, Mich.

Episodes from the History of Pulmonary Tuberculosis. W. Löffler, Dermatologica 115: 304-309 (Sept.) 1957.

Two papers published in 1878 are analyzed to show that the astute observations of a practicing physician may furnish more valuable information than the opinionated interpretations of an expert specialist. Reich, a county physician in a small Swiss community, observed 10 cases of fatal tuberculous meningitis among infants attended by a tuberculous midwife, who used her mouth to suck mucus from the newborn's air passages and blew her own breath into the child's mouth in order to promote breathing. Reich correctly interpreted this series as evidence of the infectiousness of tuberculosis, a highly debated point at that time. Sokolowski, working in a famous tuberculosis hospital, reported eight cases of "traumatic" hemoptysis in supposedly healthy persons in which manifest tuberculosis supervened. He used his observations to strengthen the prevalent opinion of his time that "phthisis" may follow traumatic hemorrhage rather than be its cause, as Laennec and others tried to teach.

Pinkus, Monroe, Mich.

Epidermodysplasia Verruciformis. W. Lutz, Dermatologica 115:309-314 (Sept.) 1957.

A case is reported which supports the view that epidermodysplasia verruciformis is related to verruca vulgaris plana and is a disseminated verrucosis developing in predisposed skin.

Pinkus, Monroe, Mich.

Inhibition of Melanin Formation by Human Epidermis. P. H. Magnin and S. Rothman, Dermatologica 115:315-320 (Sept.) 1957.

Inhibition of melanin formation by epidermal extracts is greater than can be accounted for by their sulfhydrl content. Unknown substances must be responsible for 30% to 40% of the observed inhibition.

Pinkus, Monroe, Mich.

Concerning the Etiology of Pemphigus and Dermatitis Herpetiformis. A. Marchionini and T. Nasemann, Dermatologica 115:320-333 (Sept.) 1957.

From a review of the literature the authors conclude that the majority of facts speak against a viral etiology of pemphigus and Duhring's disease. Their own efforts to demonstrate the existence of a pemphigus virus failed.

Pinkus, Monroe, Mich.

Mucous Membrane Lesions in Pringle's Disease. A. Midana and F. Ormea, Dermatologica 115:333-344 (Sept.) 1957.

A 16-year-old boy presented the typical facial lesions of "adenoma sebaceum" of Pringle. In addition, there were tumors resembling molluscum pendulum and cutaneous horns. There were extensive papillomatous tumors of the mucous membranes of the lips, cheeks, tongue, gums, and hard and soft palates. At autopsy similar lesions were found in the larynx, pharynx, esophagus, stomach, and terminal ileum.

Pinkus, Monroe, Mich.

Histology of Cutaneous Reactions Caused by Light. G. Miescher, Dermatologica 115: 345-357 (Sept.) 1957.

Epidermal cytotoxic alterations characterize the classical reaction of normal skin provoked by short ultraviolet rays. In contrast, long ultraviolet rays produce an injury of the capillaries

with necrosis of endothelial cells. Visible light and infrared rays have a pure heat effect and produce necrosis. Photodynamic substances, if applied to the skin surface, favor the development of toxic epidermal lesions. If brought to the skin by the blood stream, they provoke edema, inflammation, and necrosis in the cutis. Photoallergic reactions may be of the urticarial or the eczematoid delayed type.

PINKUS, Monroe, Mich.

CUTANEOUS RETICULOENDOTHELIOSIS IN WHIPPLE'S DISEASE. E. RUTISHAUSER and A. DE WECK, Dermatologica 115:358-373 (Sept.) 1957.

Two cases of intestinal lipodystrophy are reported in which there was associated nodular reticuloendotheliosis of the subcutis. There was reticulohistiocytic and endothelial proliferation leading to sclerosis and nodular hyalinosis, especially of the fat tissue, and to hyalinosis of vessels of all calibers.

PINKUS, Monroe, Mich.

EXPERIMENTAL ACANTHOSIS PRODUCED BY TAR AND HYDROCARBONS. F. SCHAAF, Dermatologica 115:374-381 (Sept.) 1957.

Application of crude coal tar and of various fractions and related hydrocarbons to the skin of the flank of the guinea pig produced variable degrees of acanthosis. The neutral fraction boiling below 250 C and the residue produced acanthosis, while acid and alkaline components were inactive. Pyrene in 5% solution also produced acanthosis, while toluene, indene, α-methylnaphthalene, fluorene, carbazole, anthracene, and chrysene did not.

PINKUS, Monroe, Mich.

AN UNUSUAL CASE OF PSEUDOXANTHOMA ELASTICUM. R. SCHUPPLI, Dermatologica 115: 382-386 (Sept.) 1957.

A 55-year-old woman presented clinically and histologically typical lesions of pseudoxanthoma elasticum on her neck. She complained of burning pain in the skin of her cheeks, which were erythematous and thickened and resembled orange peel. Histologic examination revealed increase and partial homogenization of elastic fibers in the cutaneous papillae, similar to that found in Miescher's elastosis intrapapillaris. There was, however, no inflammatory reaction or tendency of the fibers to be extruded through the epidermis.

PINKUS, Monroe, Mich.

STUDIES ON PATCH TESTS FROM THE POINT OF VIEW OF CUTANEOUS ALLERGY: THE PROBLEM OF EXPERIMENTAL CONTACT DERMATITIS. E. SIDI, Dermatologica 115:387-405 (Sept.) 1957.

The patch test, introduced by J. Jadassohn in 1895, remains the only precise tool for the diagnosis and experimental investigation of contact dermatitis. The author's detailed discussion of the problems involved must be read in the original article.

PINKUS, Monroe, Mich.

ROOF-SHINGLE-LIKE DYSTROPHY OF THE NAIL PLATE AS AN EXAMPLE OF RHYTHMIC PROCESSES IN THE GROWTH OF THE NAIL. A. STÜHMER, Dermatologica 115:428-432 (Sept.) 1957.

A peculiar modification of the surface of finger nails is described in which short longitudinal ridges form a pattern resembling the shingles on a roof. This alteration was observed in cases of scleroderma, psoriasis, and senility. It is explainable as the product of rhythmic changes in the formation of the nail.

PINKUS, Monroe, Mich.

ON THE NATURE OF THE MITSUDA AND THE KVEIM REACTION. R. KOOIJ AND T. GERRITSEN, Dermatologica 116:1 (Jan.) 1958.

The Mitsuda reaction, using material made from lepromatous tissue, is usually positive in patients with tuberculoid leprosy and negative in those with the lepromatous type. Kooij and Gerritsen found that lepromatous tissue was not necessary to produce this reaction, since suspensions of normal liver particles also had a similar effect.

Evidence is presented that in the Mitsuda reaction we are dealing with a sarcoid or tuberculoid type of foreign-body reaction or an isomorphic phenomenon. This conclusion is further supported by the finding that, with Kveim antigen, positive reactions are obtained in patients with tuberculoid leprosy. It is considered that the Kveim reaction is an expression of a sarcoid mode of reaction in certain persons.

MONASH, Miami, Fla.

IDENTIFICATION OF MICROSPORON FELINEUM FOX AND BLAXALL BY THE ADDITION OF AN EXTRACT OF EARTH TO THE CULTURE MEDIUM. P. WENK, and H. GELEICK, Dermatologica 116:188-192 (March) 1958.

In 1952, Van Breuseghem showed that the addition of earth to the culture medium resulted in an increased production of typical reproductive organs in fungus cultures and the formation of new macroconidia in pleomorphic organisms. The authors have used this method in the form of a boiled and filtered extract of earth added to the culture medium to assist in the identification of organisms obtained from a patient with tinea capitis and from an infected cat. Owing to lack of macroconidia, identification was impossible. When the extract of earth was added to the culture medium, the center of the fungus culture showed the macroconidia typical of Microsporon felineum Fox and Blaxall.

MONASH, Miami, Fla.

ROSACEA-LIKE TUBERCULID OF LEWANDOWSKY. W. G. VAN KETEL, Dermatologica 116:201-210 (March) 1958.

The author examined clinically and histologically 55 cases of rosacea, 6 of which could be considered clinically to be rosacea-like tuberculid of Lewandowsky. It was impossible to differentiate the two types of cases from the standpoint of histologic picture or tuberculin reaction. Many clinically typical cases of rosacea showed a tuberculoid or transitional structure, whereas, half of the clinically typical rosacea-like tuberculid cases showed a nonspecific reaction histologically. In two of the latter cases the localization of the lesions shifted from the sides of the face to the center and were then clinically indistinguishable from rosacea. The author concludes that it is impossible to constitute effective criteria for distinguishing rosacea from Lewandowsky's "rosacea-like tuberculid."

MONASH, Miami, Fla.

INSECT VIRUSES AND THEIR STRUCTURE. KENNETH M. SMITH and ROBLEY C. WILLIAMS, Endeavour 17:12 (Jan.) 1958.

This article describes fundamental research carried out in the study of insect viruses. Even though the information may not be directly applicable to other types of viruses, it is of importance in broadening our knowledge and understanding of the entire field of virology. The authors have found both intranuclear and intracytoplasmic viruses. The intranuclear viruses usually attack the skin, while the intracytoplasmic viruses usually attack the intestine. Some of the viruses are found enclosed in polyhedral-shaped bodies, some of which have been shown to be of crystalline structure.

Most of these viruses are spread by the ingestion of infected food; there is also evidence that these viruses are passed through the egg to succeeding generations. Some viruses have been shown to remain dormant even through successive generations, only then to become activated and become pathologic to their insect host.

A phenomenon noted during cross inoculation studies was the development of a virus disease different from the one with which the host was inoculated. This suggests one means by which a latent virus can be activated.

Using the electron microscope, shadowing techniques, and geometric models, the authors were able to demonstrate for the first time the geometrical form of a virus. The particular virus studied was found to be an icosahedron.

NORINS, Chicago

URTICARIA PAPULOSA CHRONICA. O. BRAUN-FALCO and U. M. VON EICKSTEDT, Hautarzt 8:534-540 (Dec.) 1957.

Through observation of 12 adult patients with urticaria papulosa chronica the paper points out the clinical, differential diagnostic, and histological criteria which distinguish the disease from other chronic pruriginous and papular-urticarial eruptions. The authors feel that disturbances in the gonadal function are of pathogenetic significance.

BULEY, Champaign, Ill.

THE DIFFERENTIAL DIAGNOSIS OF ACNE URTICATA (KAPOSI), ACNE EXCORIÉE DES JEUNES FILLES (BROCQ), AND NEUROTIC EXCORIATIONS. K. SALFELD, Hautarzt 8:546-549 (Dec.) 1957.

The author attempts to establish evidence for the separation of the three dermatoses as nosologic entities.

BULEY, Champaigne, Ill.

THE VIROLOGICAL DIAGNOSIS OF ECZEMA HERPETICATUM (HERPETIFORME) KAPOSI. T. NASEMANN and U. SCHNYDER, Hautarzt 8:549-552 (Dec.) 1957.

A case of eczema herpeticatum is described, and the various methods of virological diagnosis are discussed. These include (1) the inoculation of the rabbit cornea, (2) the histological examination of the infected rabbit cornea, (3) the culture of vesicle contents and infected cornea material in the chorioallantoic membrane of the chick egg, (4) electron microscopy, and (5) serological examination by complement-fixation reaction. In the cited case, the authors could demonstrate that the infantile eczema was secondarily infected by the virus of herpes simplex, the source of which was a primary aphthous stomatitis.

BULEY, Champaign, Ill.

THE RELATIONSHIP BETWEEN HEMIATROPHIA FACIEI AND SCLERODERMA. S. JABLONSKA, B. LUKASIAK, and B. BUBNOW, Hautarzt 9:9-15 (Jan.) 1958.

The close pathogenetic relationship between facial hemiatrophy and scleroderma is evidenced by the frequent occurrence of both diseases in the same patient and their obvious morphological similarity. Both diseases, however, are distinct nosological entities which can be distinguished by their clinical appearance, by the histological changes, and by the determination of chronaxy as a criterion for irritability. In facial hemiatrophy the chronaxy values are normal, while they are increased in all cases of scleroderma, thus indicating a diminished excitability.

BULEY, Champaign, Ill.

THE SYNDROME OF ANGIOKERATOMA CORPORIS DIFFUSUM AND ITS CUTANEOUS MANIFESTATIONS. M. RUITER, Hautarzt 9:15-19 (Jan.) 1958.

Reviewing the bibliography of the past 10 years and adding his own observations, the author points out the probability that angiokeratoma corporis diffusum is a dermadrome of a general disturbance in the phosphatid metabolism.

BULEY, Champaign, Ill.

THE SWEAT DUCT IN THE STRATUM CORNEUM SEEN IN MICROSCOPIC EXAMINATION IN VIVO. FRANZ EHRING, Hautarzt 9:25-29 (Jan.) 1958.

Histological examinations of the living skin render it possible to examine, in its natural state, that portion of the sweat duct which is embedded in the stratum corneum. In this manner, size and shape, as well as mode and speed of regeneration of the duct, can be determined.

BULEY, Champaign, Ill.

JAPANESE RICE AS A DIAGNOSTIC MEDIUM FOR YEAST. H. RIETH, K. ITO, and C. SCHIRREN, Hautarzt 9:36-38 (Jan.) 1958.

Culture plates prepared from Japanese rice, agar-agar, and water are a valuable aid in the diagnosis of Candida albicans. Within 16 to 48 hours the characteristic chlamydospores can be identified in the culture. The medium also serves well in the differentiation of other yeast organisms.

BULEY, Champaign, Ill.

Abnormal Sweat Electrolytes in Patients with Allergies. David Yi-Yung Hsia, Shirley G. Driscoll, Donald Greenberg, Ting-Chien Lee, and Gilbert Lanoff. Clin. Res. 6:319-320 (April) 1958.

Sodium and chloride determinations were made of the sweat of normal and allergic persons and persons with cystic fibrosis of the pancreas. Abnormally high values were found not only in patients with cystic fibrosis but also, though not so high, in allergic persons. The results, expressed in milliequivalents per liter were as follows: normal individuals—sodium, 21.7; chloride, 19.5; allergic patients—sodium, 42.8; chloride, 30.0; patients with cystic fibrosis—sodium, 103.2, and chloride, 101.0. The sweat abnormalities were not limited to any one particular form of allergy.

Samuel Monash, Miami, Fla.

Study of the Relationship of Malignant Disease to Dermatomyositis. James T. Grace Jr. and Thomas L. Dao, Clin. Res. 6:302-303 (April) 1958.

A young pregnant woman with acute breast carcinoma developed dermatomyositis while under observation. She showed strong skin sensitivity of the immediate type to an aqueous extract of the tumor. Interruption of pregnancy and oophorectomy produced temporary tumor regression and improvement of the dermatomyositis. Subsequent tumor progression was accompanied by exacerbation of the dermatomyositis. Similar sensitivity without the development of dermatomyositis was found in tumors exhibiting unusual local reactions, such as inflammation, edema, and pronounced tenderness.

Samuel Monash, Miami, Fla.

New Radiation Technique in the Treatment of Benign and Malignant Conditions of the Skin. Sobrino De Rienzo, Arch. argent. dermat. 7:351-358 (Dec.) 1957.

The author states that the technique of dividing the total dosage of radiation necessary to eradicate a tumor with small fractions furnishes a higher index of efficiency with less damage. Hemangiomas in infants may be treated without risk of inhibiting epiphyseal growth. The author believes that cosmetically objectionable hypertrichosis may also be safely treated with radiation of this sort. Only deep penetrating radiation was used in this study, but possibly softer radiation might also be used. The dosage for carcinomas was 4500 to 6000 r; 100 r daily, 200 kv., 0.5 mm. Cu, 2 mm. Al, focus distance 45 cm. Reaction manifested by erythema appears after 2500 to 3000 r has been administered and disappears at the end of the treatment, about the 45th or 50th day. Cosmetic results are satisfactory.

Orlando Canizares, New York

Scleroderma and Dermatomyositis. Julio Borda, Arch. argent. dermat. 7:327-350 (Dec.) 1957.

This erudite and valuable article presents a summary of the author's concept of scleroderma and dermatomyositis, gained by 20 years of personal interest and study of the subject. The interrelation between these two entities is stressed. The article should be read in the original by all those interested in these subjects.

Orlando Canizares, New York

Epilating Folliculitis of the Glabrous Skin (Arnozan and Dubreuilh): A Study of 78 Cases. Pastor Fariñas and V. Pardo Castello, Bol. Soc. cubana dermat. y si. 14:7-24 (March-June) 1957.

In this study the authors report 78 cases of a type of folliculitis first described by Arnozan and Dubreuilh in 1892 and 1894. The condition is a pustular folliculitis of symmetrical distribution. The areas most affected are the legs, thighs, and forearms, but other hairy areas may be also involved. The lesions are grouped in plaques or bands with tendency to peripheral extensions. They occur in successive attacks which are extremely pruriginous. The condition causes a permanent alopecia of the affected areas. It is almost exclusively observed in white males and especially affects workers in the sugar cane plantations. From the histopathologic studies, it is concluded that the condition is due to excessive sweating, obstruction of the

follicular ostia by edema and keratin plugging, and secondarily by infection with Staphylococcus aureus. The role played by the very large and abundant eccrine sweat glands, as well as by the sebaceous glands, is emphasized.

ORLANDO CANIZARES, New York

ARSENICAL POLYNEURITIS AND INGUINAL LINES OF MEES OF TOXIC ORIGIN. A. M. PEROSIO, Prensa méd. argent. 44:1454-1457 (May 10) 1957.

The author reports a case of a woman who attempted to commit suicide with an arsenical preparation. Approximately six weeks later the patient developed a polyneuritis. Three months after the ingestion of arsenic a white transversal band 1 mm. in width appeared in all nails. This was described as leuconychia striata transversa arsenicalis by Mees in 1919.

ORLANDO CANIZARES, New York

THE SOUTH AMERICAN BLASTOMYCOSIS IN COLOMBIA. F. LONDOÑO GONZALEZ, Rev. Fac. med. (Bogotá) 25:101-118 (March-April) 1957.

The author reports seven cases of this disease observed in Bogotá. He describes a clinical variety manifested by a violaceous plaque, which is not mentioned in the classification of Aguiar Pupo. Most patients were farmers. The author stresses the fact that patients with extensive cutaneous lesions may be free of visceral changes, while others with minimal cutaneous manifestations may present severe visceral involvement.

ORLANDO CANIZARES, New York

AN EXPLANATION OF ORIGIN AND CAUSE OF CHAPPED SKIN. O. JACOBI, Berufsdermatosen 6:35-40 (Feb.) 1958.

In addition to sebum and other substances, the stratum corneum contains hygroscopic compounds which are soluble in water, ether, and methanol. These components enable the tissue to store the water essential for its physiological tasks. When they are removed, the stratum corneum loses its capacity to retain water, the water evaporates, and the skin becomes dry and chapped.

H. M. BULEY, Champaign, Ill.

EXPERIMENTAL STUDIES CONCERNING SOME DERMATOMYCOSES TRANSMISSIBLE BY ANIMALS. C. SCHIRREN and H. RIETH, Berufsdermatosen 6:31-35 (Feb.) 1958.

The authors were able to report the first incidence in Germany of Trichophyton rubrum infection in cattle. The mode of invasion of hair by dermatophytes is observed in a simple experiment. In the infection of a hair by Mycobacterium canis "penetration organs" of the magnitude of macroconidia are described.

H. M. BULEY, Champaign, Ill.

OCCUPATIONAL ASPECTS OF SOME DERMATOMYCOSES. V. A. BALABANOFF, Berufsdermatosen 6:18-31 (Feb.) 1958.

On the basis of his own observations and reports in the literature, the author surveys the various mycotic infections of the skin and their potentialities as occupational hazards.

H. M. BULEY, Champaign, Ill.

INVESTIGATIONS CONCERNING THE EFFECT OF PROTECTIVE OINTMENTS AND OF WASHING AGENTS ON THE HUMAN SKIN BY MEANS OF A MODIFIED ALKALI NEUTRALIZATION TEST. W. SCHNEIDER and H. TRONNIER, Berufsdermatosen 6:1-17 (Feb.) 1958.

By a modified Burckhardt test for the determination of alkali neutralization, the modes of action of protective creams, soaps, and shampoos are demonstrated on 11 charts. Washing agents are classified according to their action (1) on the surface of the skin and (2) on the deeper layers, which results in a swelling of the skin.

H. M. BULEY, Champaign, Ill.

ALKALI RESISTANCE AND ALKALI NEUTRALIZATION TIME. E. SCHULTHEISS, Hautarzt 9:131-135 (March) 1958.

The findings of alkali resistance ("alkali tolerance," Burckhardt) and alkali neutralization time are statistically evaluated. The determination of alkali resistance measures the capacity of the skin to swell and the ability of the cutaneous vessels to react to alkali, while alkali neutralization time refers to the buffering capacity of the epidermal proteins.

H. M. BULEY, Champaign, Ill.

BEJEL—ITS PECULIARITIES AND ITS RELATION TO SYPHILIS. A. G. KOCHS, Hautarzt 9:125-130 (March) 1958.

On the basis of the concept that bejel is a modified endemic form of syphilis, the symptomatology of the disease is discussed. Its peculiarities are thought to be due to environmental and geographic factors.

H. M. BULEY, Champaign, Ill.

DYSHIDROSIFORM ERUPTIONS AND THE SWEAT ORGAN: 1. MORPHOLOGICAL FINDINGS IN SIX PATIENTS WITH HYPERHIDROSIS AND VESICULAR ERUPTIONS OF THE PALMS AND THE SOLES. F. HERMANN, S. D. MORRILL, and M. B. SULZBERGER, Hautarzt 9:60-67 (Feb.) 1958.

The histopathological changes observed suggest that hyperhidrosis causes an increased hydration of the stratum corneum compactum. This aqueous saturation leads to a swelling of the horn cells, resulting in a blockage of some sweat ducts. The retention of sweat may then be followed by the formation of intraepidermal vesicles and miliaria-like reactions.

H. M. BULEY, Champaign, Ill.

ERYTHEMA ANULARE RHEUMATICUM. O. HORNSTEIN, Hautarzt 9:120-125 (March) 1958.

Erythema anulare (Lehndorff-Leiner) is a specific rheumatic exanthem, caused by a local antigen-antibody reaction. This is regulated by a neurovascular mechanism affecting the morphological characteristics and extent of the eruption. Its presence is of great prognostic importance, as it is usually accompanied by an involvement of the endocardium.

H. M. BULEY, Champaign, Ill.

MULTIPLE RETICULOHISTIOCYTOMAS OF THE SKIN IN CASES OF DESTRUCTIVE JOINT DISEASE. DELIA WALTHER, Hautarzt 9:78-81 (Feb.) 1958.

A case of disseminated reticulohistiocytomas associated with primary chronic rheumatic arthritis is reported. The differences found in the histological sections of five lesions biopsied at intervals over a period of a year are explained on the basis of their representing eruptive and regressive phases of the same morbid process. Reticulohistiocytomas are understood to be allergic granulomatous reactions which may occur in the course of rheumatic disease.

H. M. BULEY, Champaign, Ill.

THE ABRIKOSSOFF TUMOR (GRANULAR-CELL MYOBLASTOMA). H. REICH, Hautarzt 9:71-77 (Feb.) 1958.

On the basis of the review of an extensive bibliography, granular-cell myoblastomas are recognized as granular neuromas. The pseudoepitheliomatous proliferation often found in histological sections may lead to diagnostic errors. The term "Abrikossoff tumor" is proposed for general usage because it is "the shortest and easiest to remember."

H. M. BULEY, Champaign, Ill.

THE DEMONSTRATION OF ALKALINE PHOSPHATASE IN CAPILLARIES. C. KLINGMÜLLER, Hautarzt 9:84-88 (Feb.) 1958.

In the stereoscopic histochemical demonstration of alkaline phosphatase, it is noticed that the arterial portions of the capillary loops stain a darker black than the venous portions. The difference in the fermentative activity of both suggests significant differences in their functions under normal and pathological conditions.

H. M. BULEY, Champaign, Ill.

THE ESTERASES OF THE SCALP. G. K. STEIGLEDER, Hautarzt 9:67-71 (Feb.) 1958.

Unsaturated esterases, as demonstrated by the Gomori technique, are found throughout the epidermis of the scalp. The most intensive coloring is found in the layer between the stratum corneum and the nonkeratinized cells. This layer of maximal reaction continues deeply into the hair follicles and seems to be independent of the presence of sebum, which explains why one finds, in the fat of hair, lipid substances which do not occur in the sebaceous glands.

H. M. BULEY, Champaign, Ill.

THE HISTOPATHOLOGICAL DIFFERENTIATION BETWEEN PIGMENTED NEVI, JUVENILE MELANOMAS AND MALIGNANT MELANOMAS. H. MONTGOMERY, Hautarzt 9:52-56 (Feb.) 1958.

The difficulties in the histological diagnosis of growing pigmented and nonpigmented nevi, of juvenile melanomas, and of early malignant melanomas are pointed out. The microphoto-

graphs of sections from 10 cases with characteristic changes serve to demonstrate the important differential diagnostic criteria.

H. M. Buley, Champaign, Ill.

The Psychological Indications for Medicocosmetic Procedures. E. Niebauer and A. Wiedmann, Hautarzt 9:57-60 (Feb.) 1958.

Statistics and clinical observations point to the importance of psychological aspects in the use of cosmetic procedures. In the interest of the patient, as well as for the medicolegal protection of the physician in charge, the authors advise routine consultations with a psychologist prior to cosmetic operations.

H. M. Buley, Champaign, Ill.

# Announcements

**Meeting of the Academy.**—The 17th Annual Meeting of the American Academy of Dermatology and Syphilology will be held Dec. 6-11, 1958, at the Palmer House in Chicago.

Special Courses will be held as before in Histopathology (Inflammatory Dermatoses, and Reticuloendothelial and Alterative Dermatoses); Mycology, (Superficial and Deep Mycoses); X-Ray and Radium; Bacteriology and Virology; Special Problems in Dermatohistopathology; Anatomy and Embryology of the Skin; Application of Research Methods to Dermatology, which has been extended to a two-day course; the addition of a new Special Course, Fundamentals of Allergy; Cutaneous Surgery, formerly Surgical Skin Planing. The Special Course on Cutaneous Surgery will again be limited in attendance to 80 for each day, and to accommodate those unable to register for the course part of the material will be covered in a Symposium on Thursday morning, Dec. 11.

Changes have been made in the Informal Discussion Groups. Tickets for these groups are to be purchased at the registration desk for same day *only*. No preregistrations accepted.

Dr. G. A. Grant Peterkin of Edinburgh, Scotland, the invited foreign guest speaker, will give the Sunday lecture entitled "The Changing Pattern of Dermatology." The Monday Scientific Sessions will cover the subject of Trends in Radiology, the speakers being Drs. Anthony C. Cipollaro and Howard B. Latourette. The John E. Rauschkolb Memorial Lecture on Tuesday night will be given by Dr. Cornelius P. Rhoads entitled "Research in Cancer."

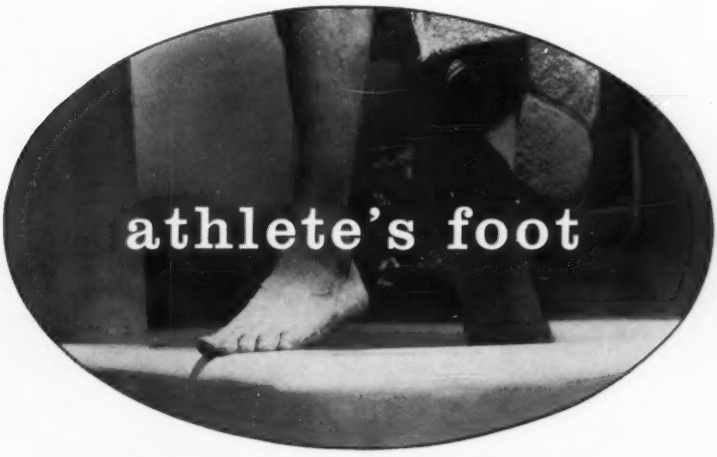
As usual there will be excellent Technical and Scientific Exhibits. There is still available space for Scientific Exhibits and anyone who is considering such a presentation should communicate without delay with Dr. Frederick B. Malkinson, 950 E. 59th St., Chicago 37.

# Books

**Medical Mycology Including Laboratory Technique and Therapeutic Recipes.** By N. C. Dey, B.Sc., M.B.B.S (Cal.), D. Bact. (Manchester), F.D.S. (Lond.). Price, $5.00. Pp. 127. S. K. Seal, Pressagents Private, Ltd., 2 Cornwallis St., Calcutta-6, India, 1958.

This new book on medical mycology in English, from Calcutta, points to the growing world-wide interest in fungus diseases. The author, a pathologist and mycologist, has for years been interested in and has written on cutaneous mycology—this book is the result of that experience. Considerable attention is given to fundamentals such as classification, definition of terms, nomenclature, synonyms, historical introductions, etc. The various diseases are presented in didactic form. For data on diseases such as North American blastomycosis, which are not observed in India, the author borrowed from pertinent literature. Special sections are devoted to items such as solvents and stains, collection of material for examination, culture media, and topical therapy. The book is well-produced and amply illustrated with good reproductions—some in color—drawings, and charts, and it is well indexed.

The book merits success in the author's aim to be helpful to students and practitioners in India.

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**REFERENCES:** 1. Howell, C. M.: N. Carolina M.J. 18:322, 1957. 2. Brandt, R., and Dexter, H.: J. Invest. Dermat. 15:163, 1950. 3. Brandt, R., and Dexter, H.: Ibid. 19:409, 1952. 4. Brandt, R., and Szolomejer, W.: A.M.A. Arch. Dermat. 76:241, 1957.

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**References:** 1. Sokoloff, O. J.: Meprobamate (Miltown) as adjunct in treatment of anogenital pruritus. A.M.A. Arch. Dermat. **74**:393, Oct. 1956. 2. LeVan, P.: Clinical dermatologic studies of four chemically different tranquilizers. Clinical Med. **4**:1089, Sept. 1957.

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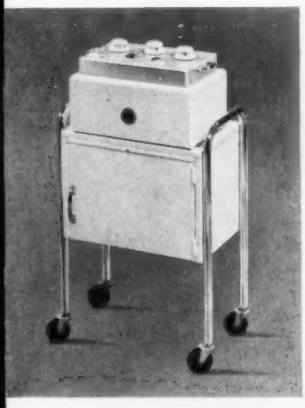

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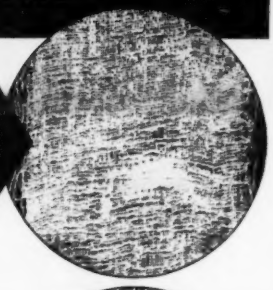

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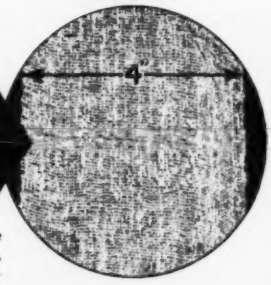


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Use of Banthine is described[1] in Wiener's recent text: "The main indication for dermatologic use is hyperhidrosis, but it has also been found useful in the control of normal sweating, in dyshidrotic vesicular eruptions, in intertrigo, in contact dermatitis, and in suppurative hydradenitis axillaris. The average initial adult dose is 50 mg. administered orally or parenterally. More or less may be given three times daily, but the daily total should not exceed 450 mg. The daily dosage in the treatment of hyperhidrosis is 100 to 200 mg., but higher doses may be necessary. . . . Following a dose of 100 mg., dryness of the palms usually sets in after thirty to forty-five minutes and lasts four to five hours. . . . The clinical reports have so far been favorable."

Banthine is also recommended[3] for the hyperhidrosis occurring with *Tinea pedis*.


1. Wiener, K.: Systemic Associations and Treatment of Skin Diseases, St. Louis, The C. V. Mosby Company, 1955, pp. 329; 458-459.
2. Perry, D. J.; Mount, G. D., and Browne, B. W.: The Effect of Varying Oral Dosages of Banthine, Pro-Banthine and Prantal on the Galvanic Skin Response, J. Invest. Dermat. *28*:239 (March) 1957.
3. Olansky, S., and Callaway, J. L., in Modern Medicine 1958 Annual (Part 1): Management of Superficial Infections, Minneapolis, Modern Medicine, 1957, p. 46.


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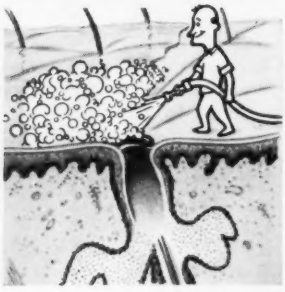

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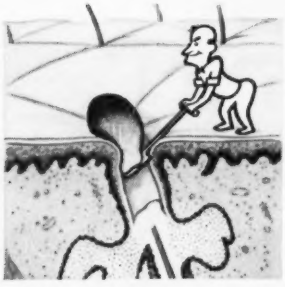
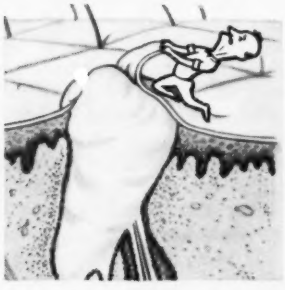


- Penetrate and soften comedones, unblocking the pores and facilitating removal of sebum plugs.



## Fostex dries and peels the skin

- The Sebulytic base of Fostex dries and promotes peeling of the skin . . . actions enhanced by the keratolytic effects of micropulverized sulfur and salicylic acid.

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for maintenance therapy to keep skin dry and substantially free of comedones.

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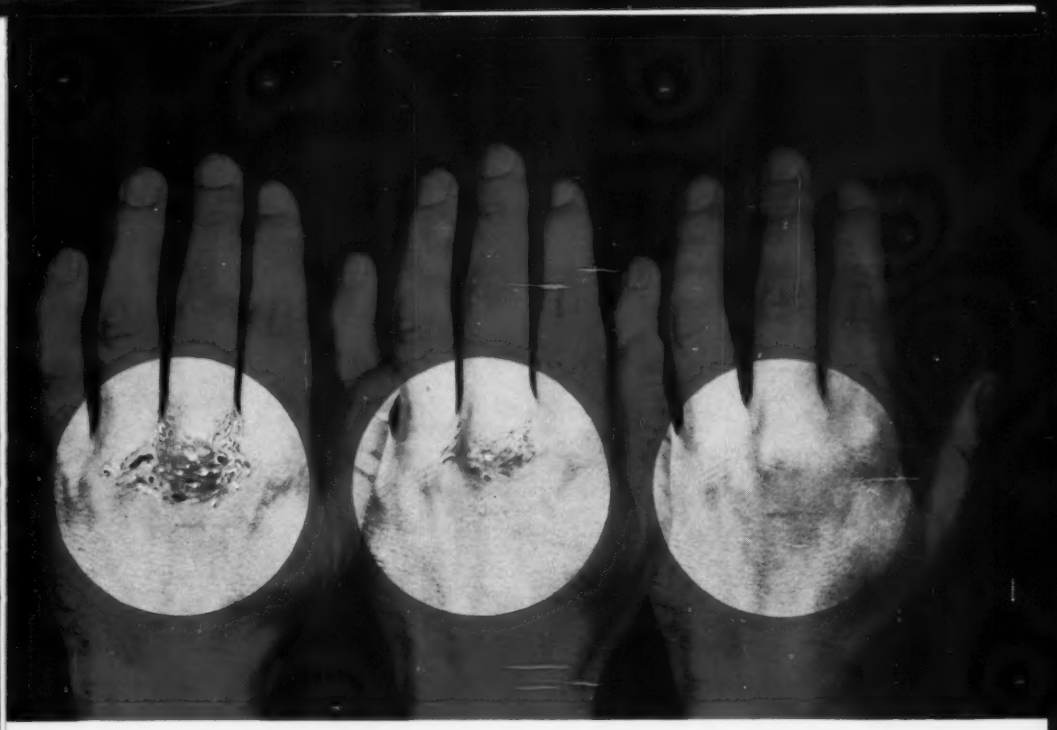

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1. Howell, C. M., Jr.: Am. Pract. & Digest Treat. 8:1928, 1957.
2. Frank, L.: A.M.A. Arch. Dermat. 75:876, 1957.
3. Welsh, A. L.: Internat. Rec. Med. 169:775, 1956.
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5. Janssens, J.: Le Scalpel 111:69, 1958.
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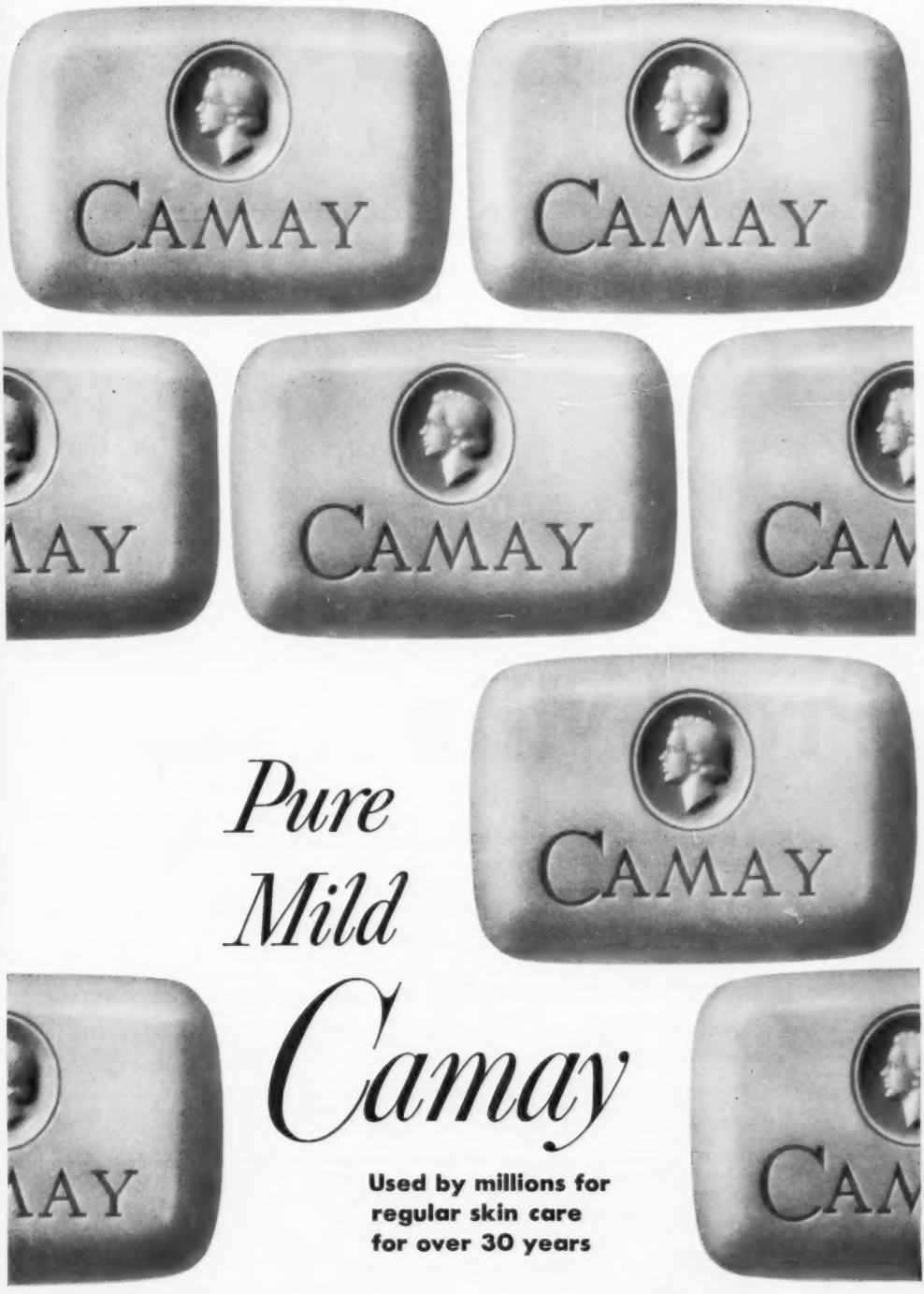


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*Peck, S. M.; Traub, E. F., and Spoor, H. J.: A.M.A. Arch. Dermat. & Syph. *67*:263, 1953.

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# CORTROPHIN-ZINC

## in Allergies

*(Corticotropin-Alpha Zinc Hydroxide)*

**Description:** The new electrolytic Cortrophin-Zinc is indicated in most allergic manifestations. Pollen, drug and food reactions, as well as toxic plant dermatoses are significantly improved. Because of prolonged activity, frequent injections are not necessary. Each injection is effective for at least 24 hours, and in milder cases, for 72 hours.

**Characteristics:** New Cortrophin-Zinc provides corticotropin of unsurpassed purity with low foreign protein content. This reduces the risk of sensitization reactions.

Since about 5% of the corticotropin is uncombined, onset of clinical response is rapid. But the balance, present as a complex of alpha zinc hydroxide, provides a prolonged action so that the effective time span of a single dose is usually several days. Injection of the new electrolytic Cortrophin-Zinc is virtually painless.

**Pharmacology:** A potent stimulator of cortical activity, Cortrophin-Zinc *does not depress* functioning of the suprarenal glands. Unlike the corticosteroids, adrenocorticotropic hormone arouses the adrenal glands to produce *natural* steroids in natural proportions. In a 5-year study of patients on ACTH therapy, no case of adrenal *or pituitary* depression or atrophy has been observed.

Because Cortrophin-Zinc is virtually painless on injection and its prolonged action obviates frequent injections, it is now practicable to use Cortrophin-Zinc in most of the indications where formerly reliance has been on corticosteroids. This freedom from apprehension of deleterious depressive effects permits clinical use of valuable hormone therapy on a broader scale than has been possible heretofore.

**Clinical Uses and Dosage:** The many published reports on the use of Cortrophin-Zinc as well as ACTH in thousands of patients indicate its value in over 100 disorders. Most responsive have been: allergies and hypersensitivities; rheumatoid arthritis, bronchial asthma, serum sickness and inflammatory skin and eye diseases.

Dosage should be individualized, but generally initial control of symptoms is obtained with a single injection of 40 Units of Cortrophin-Zinc daily until control is evident. Maintenance dosage is generally 20 Units (or less) twice a week.

Use of Cortrophin-Zinc with oral steroids is now recommended as a safety measure to supply the important suprarenal stimulation and lessen the hazard of atrophy. The periodic use of Cortrophin-Zinc is advocated with all steroid analogs, such as cortisone, hydrocortisone, prednisone, prednisolone, methylprednisone and triamcinolone.*

**Supply:** 5-cc vials containing 40 and 20 U.S.P. Units of corticotropin per cc; 1-cc ampuls containing 40 and 20 U.S.P. Units of corticotropin, with sterile disposable syringes.

*Write for complete literature and bibliography containing specific dosage schedules to:

*Medical Department*

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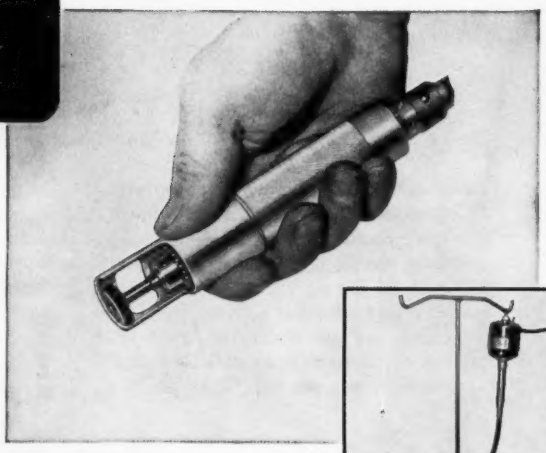
The Stryker

# WIRE BRUSH UNIT for SKIN PLANING



Motor can be suspended at a suitable height to be free of "drag" on the flexible cable.

## 6 Valuable Features of the STRYKER WIRE BRUSH UNIT

- GUARD REDUCES BLOOD SPLASH—yet permits clear view of planing area.
- HANDPIECE CANNOT BE DAMAGED by accidentally catching the brush in gauze, gloves, or hair.
- 22,000 RPM'S AT FULL SPEED—for most effective abrasion, yet lower speeds are available.
- HANDPIECE IS HAND-CRAFTED OF ALUMINUM—with stainless steel bearings for cool operation and long life. Can be cold sterilized or autoclaved.
- SENSITIVE, VARIABLE SPEED footswitch control.
- STAINLESS STEEL JACOBS CHUCK—firmly holds any brush, or abrasive wheel.

## PRICES

Stryker Wire Brush Unit ..... $219.00

Consists of: Motor and cable, handpiece, variable footswitch and carrying case (foam rubber lined.)

Less carrying case ..... $205.00

Wire Brushes—Order Separately.

Standard Small Wire Brushes (2mm. rounded cutting side) ¾" diameter in soft, regular, or coarse abrasion, each ..... $6.00

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No. 1310 Standard Mayo Table. Chrome plated, 40 lb. base, holds accessories and provides mount for motor above 5 ft. $110.00

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POLARAMINE REPETABS, 6 mg., bottles of 100 and 1000.
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Acid Mantle-Hydrocortisone

CREME AND LOTION—pH 4.6

ABATES INFLAMMATION AND RESTORES NORMAL SKIN ACIDITY

"Susceptibility to infection by bacteria is widely held to be due to the removal of the antibacterial 'acid mantle' of the skin and its displacement by an abnormal 'alkaline mantle'."—Fabricant, N. D.: A. M. A. Arch. Otolaryn. 65:11, 1957.

Supply—⅛%, 1% and 2½% hydrocortisone in either Creme (⅛ oz., 1 oz., 2 oz., 4 oz. tubes and 1 lb. jars) or Lotion (½ oz., 1 oz., 2 oz., 4 oz. squeeze bottles and pt. bottles).

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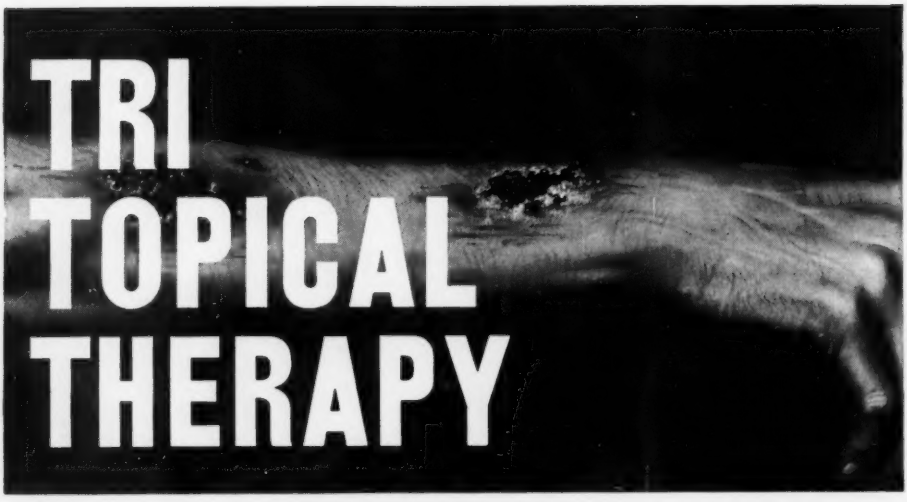


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containing MYCOSTATIN, an antifungal antibiotic specific for localized *Candida* (Monilia) *albicans* infections and an agent of choice for treatment or prevention of cutaneous monilial infections.

containing FLORINEF, a potent topical antipruritic and anti-inflammatory agent known to combat local reactions to fungal, bacterial, chemical and physical irritants.

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Apply sparingly and lightly 2 to 4 times daily, as indicated. When improvement is observed reduce frequency of administration.

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- **Absorbs skin exudates**
- **Soft creamy texture**
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- **More soothing (because it contains Aveeno Colloidal Oatmeal)**
- **Anti-bacterial**

**AVEENO® OINTMENT** is compatible with all medicaments that may be added to Lassar's Paste. Typical compatibilities are:

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Active Ingredients: Aveeno® Colloidal Oatmeal, zinc oxide and 0.5% hexachlorophene in an emollient base.

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AVEENO OINTMENT is now available in a 4 oz. economy size tube as well as the 1 oz. tube.

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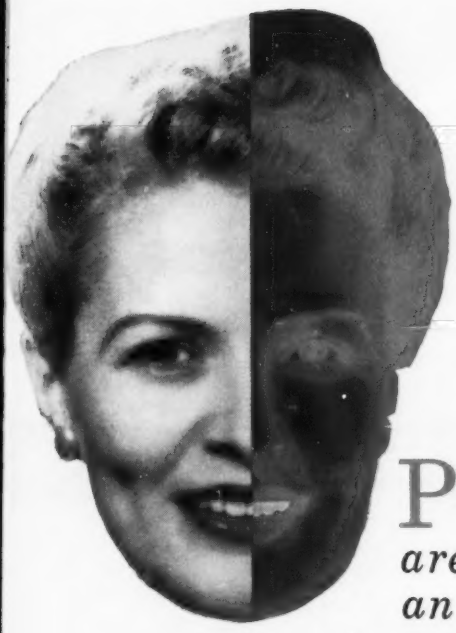

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*are half personalities, for an uncomfortable person is only one half a personality*

# EPIDOL®

*will help to restore the psoriatics' appearance and self-confidence.*

EPIDOL is a clear, *adhesive, non-greasy,* rapidly drying, improved Wright Liquor Carbonis Detergens plus Salicylic Acid 3%.

EASY to apply. Applicator comes with every bottle.

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SUPPLIED: Bottles with applicators: 3 fl. oz.—6 fl. oz.

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# normal protective cover

Normal skin has an acid pH range between 4 and 6

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**CREME or LOTION pH 4.2**

In housewives' eczema and industrial dermatitis, promptly restores and maintains the normal protective acidity of the skin. Active ingredient is aluminum acetate in specially formulated bases.

"The importance of a measure designed to return the pH of the skin quickly to its normal values after exposure to soap and alkalies is amply borne out..."

—Gross, P., et al.: A. M. A. Arch. Dermat. & Syph. 70:94,1954

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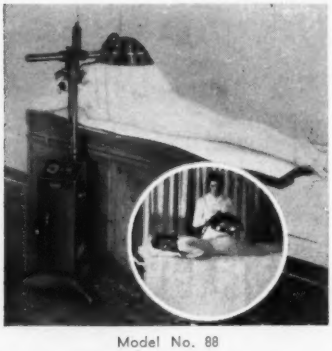

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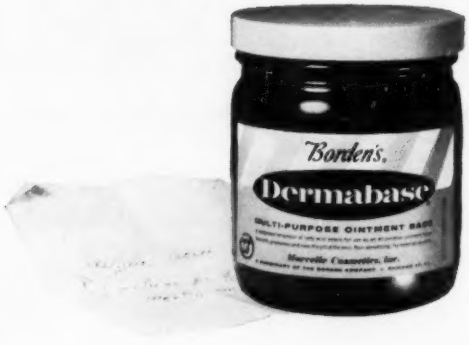


*"Even where a specific drug action is required, success of the treatment still may depend largely upon the proper choice of a vehicle."*

Carney, R. G.: The pharmacology of dermatological therapy. South Dakota J. Med. & Pharm. 9:377, 1956.

Devoid of all known irritants and sensitizing agents, including lanolin derivatives and perfumes

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Stabilized emulsion at normal skin pH maintains acid mantle of skin and close contact of medicament.

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FLURO-ETHYL is a solution of Ethyl-Chloride and Dichlorotetrafluoro-ethane which has been demonstrated to be useful as a topical refrigerant for use in plastic surgical skin planing and as an agent to produce local anesthesia for minor surgical procedures. It contains 75% Dichlorotetrafluoro-ethane and 25% Ethyl-Chloride, and when applied topically to the skin, produces rapid refrigeration and anesthesia to the desired depths of the skin.

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## in a wide variety of PYODERMAS

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In a recent study[1] of 53 patients with various types of pyodermas, the use of BACIMYCIN Ointment "... resulted in a cure rate of 88%...." Impetigo, infectious eczematoid dermatitis, atopic eczema, secondary infections superimposed on dermatitis venenata, and folliculitis were among the common skin infections that showed marked improvement with BACIMYCIN therapy.

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Supplied in ½ oz. tubes for prescriptions; in 100 gm. jars for hospital use; in ⅛ oz. tubes for ophthalmic use. Also supplied as BACIMYCIN with Hydrocortisone, ⅛ oz. tube with applicator tip.

Literature and samples on request.

1. Greenhouse, J. M., and Ryle, W. C.: A.M.A. Arch. Dermat. & Syph. 69:366 (March) 1954.

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... *Practical Medical Mycology*
By J. Walter Wilson, M.D.
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Arch D & S 59:414, April 1949

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